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STUDIES IN REGIONAL HEPARINIZATION*

II. Artificial-Kidney Hemodialysis without Systemic Heparinization — Preliminary Report of a Method Using Simultaneous Infusion of Heparin and Protamine

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SAN FRANCISCO

WHEN artificial-kidney hemodialysis is performed, the patient is ordinarily heparinized to prevent activation of the coagulation mechanism as the blood passes through the extracorporeal circuit. The use of this anticoagulant is largely responsible for the fact that active uncontrollable bleeding, particularly from the gastrointestinal tract, remains the only absolute contraindication to the use of the artificial kidney.[1-4]

In the first part of this report[5] it was demonstrated that a very prolonged clotting time could be achieved in a part of the circulation without appreciably affecting the clotting time in the remainder of the circulation. One of us (E.R.S.) suggested that this procedure could be applied to uremic patients in whom active bleeding contraindicated hemodialysis. A technic was devised, therefore, to permit continuous controlled addition of heparin to the patient's blood on its way to the artificial kidney. Simultaneously, the neutralizing dose of protamine is added automatically to the blood on its return into the patient. Thus, the patient's ability to clot is maintained unchanged without the danger of clot formation in the extracorporeal circuit.**

It is the purpose of the present communication to describe our method of regional heparinization and to present preliminary results in a nephrectomized dog and in 2 patients in whom potential bleeding made systemic heparinization hazardous.

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**After this manuscript had been completed it was discovered that Kolff[6] had already suggested the need for such a method.

MATERIALS AND METHODS

Heparin (Upjohn heparin sodium, 10 mg. per milliliter) and protamine sulfate (Lilly, 1 per cent) were used in this work. Hemodialysis was carried out by means of the Stanford University Hospitals artificial kidney (Brigham–Kolff type) built by Olson.††

In the first part of this communication it is reported that a suitable ratio of heparin to protamine for regional in vivo heparinization is 5:6 with the lots used. To a 500-ml. bottle of 5 per cent dextrose in water the appropriate amount of heparin is added so that with an administration rate of approximately 1 to 1.5 ml. per minute adequate heparinization is achieved in blood flowing through the artificial kidney. For every 5 mg. of heparin added, 6 mg. of protamine is added to a second 500-ml. bottle of 5 per cent dextrose in water.

It was found that levels of heparinization neutralized by 10 microgm. of protamine per milliliter would give adequate fluidity to the blood. Since hemodialysis is usually carried out at blood-flow rates of 250 to 300 ml. per minute, it is necessary to add approximately 2 or 3 mg. of heparin to the blood per minute. We have prepared the heparin solution to contain 1.4 mg. per milliliter (800 mg. added to 500 ml. of 5 per cent dextrose in water). The protamine solution is then made to contain 1.7 mg. per milliliter (960 mg. added to 500 ml. of 5 per cent dextrose in water). A wide range of concentrations can be used, but because patients placed on the artificial kidney are oliguric, it is desirable to restrict the fluid intake as much as possible. With the use of this relatively high concentration, it is possible to restrict the intake to less than 1200 ml. total and to keep the dialysis going at least six or seven hours.

The heparin enters the extracorporeal circuit through a 22-gauge needle inserted in the direction of blood flow through a rubber sleeve placed over

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the arterial cannula at a point 3 cm. distal (relative to the patient) to the insertion of the cannula into the radial artery (Fig. 1). Protamine is added in a similar manner in the direction of blood flow at a point about 3 cm. distal (relative to the patient) to the entrance of the venous catheter.

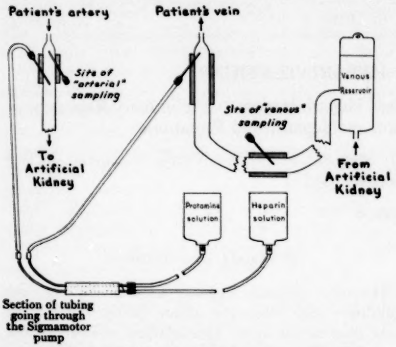

FIGURE 1. *Technic of Infusion and Sampling.*

The slow, equal and constant rates of simultaneous infusion of heparin and of protamine despite differences in end pressures are achieved by means of a Sigmamotor pump* and paired infusion sets. The part of the infusion set going through the pump consists of a pair of sterile No. 12 Fr. catheters passing through a section of gum-rubber tubing as described in the first part of this report.[5]

The following simplification of the protamine titration test developed by one of us (H.A.P.)[7] is used to determine the presence of adequate heparinization of the blood in the extracorporeal circuit and the achievement of adequate heparin neutralization in the systemic circulation.

With the same lot of protamine as is to be used during dialysis, dilutions of protamine are made with isotonic saline solution to obtain concentrations of 5, 10 and 15 microgm. per 0.1 ml. These are freshly prepared before the start of each hemodialysis. Six rows of test tubes, 12 by 75 mm., containing 18 tubes per row, are set up. In this way sufficient tubes are available to perform 18 separate titrations during the dialysis. Two rows, numbered 1 and 2, are used for the arterial-inflow samples and 4 rows, numbered 1 to 4, for the venous-return samples (see Table 1); 0.1 ml. of saline solution is carefully pipetted into each of the tubes of rows numbered 1. Rows numbered 2 receive 5 microgm. of protamine solution per tube. Rows numbered 3 and 4 receive 10 and 15 microgm. of protamine solution per tube respectively.

Arterial samples are obtained through a needle inserted into the same rubber sleeve covering the origin of the arterial cannula through which the heparin needle is placed (Fig. 1). This arterial sampling needle points *against* the direction of blood flow and, when not in use, can be occluded with a stylet. Its point is located about 5 cm. proximal to the point of the heparin needle. In this way heparin contamination of the arterial sample is avoided.

Venous-return blood is sampled at any convenient point in the venous cannula between the plastic reservoir bag and the point of protamine entry and in such a way that protamine contamination of the samples does not occur (Fig. 1).

Titration is carried out as follows: 1 ml. of arterial-cannula blood is added to 1 tube from each of the 2 "arterial" rows of tubes. The tubes are then inverted once to mix their contents and are kept at room temperature. They are inspected at fifteen minutes (as described in the first part of this report[5]), to see which ones are clotted. Similarly, 1 ml. of venous-cannula blood is added to 1 tube from *each* of the 4 "venous" rows.

TABLE 1. *Results of Protamine Titration in Case 1 (June 5, 1956).*

SYSTEMIC CIRCULATION
Arterial-cannula samples

Duration of Dialysis (min.)	Rows 1 & 2: Protamine conc. micrograms/ml 0	5
3	−	+
20	+−	+
50	+	+
106	+	+
142	+	+
226	+	+
293	+	+
323	+	+

+ = *Clot at 15 min.*
− = *No clot at 15 min.*

EXTRACORPOREAL CIRCUIT
Venous-cannula samples

Duration of Dialysis (min.)	Rows 1–4: Protamine conc. micrograms/ml 0	5	10	15
6	−	−	−	−
23	−	−	−	−
32	−	−	+	+
55	−	−	−	+
80	−	−	−	−
107	−	−	−	−
123	−	−	+	+
147	−	−	−	+
167	−	−	+	+
198	−	−	−	+
243	−	+−	+	+
260	−	−	+	+
290	−	−	+	+
320	−	−	+	+
352	−	−	+	+

Technic of Dialysis

Hemodialysis is carried out in the standard manner.[1,2] The artificial kidney is primed with citrated bank blood. The arterial and venous cannulae are each filled with a mixture of saline solution and 5 mg. of heparin. Rotation of the artificial-kidney drum is begun, and the Sigmamotor pump is started at a previously determined rate that delivers an amount of heparin sufficient to anticoagulate 250 to 300 ml. of blood per minute (as described above). For the first few minutes the arterial inflow is limited to about 100 ml. per minute. This serves to compensate for the venospasm that usually limits the venous return at the start of dialysis. In addition, the excessive initial regional heparinization thus accomplished is safer than an initial heparin deficiency (see Table 1).

Five to ten minutes after the start of dialysis, the arterial inflow is gradually raised, and the remainder

*T-6S unit, Model 142X Revco Zero-Max Speed Changer, 1/6-h.p. electric motor, 110 v., 60 cy., 1 phase, available from Sigmamotor, Incorporated, Middleport, New York.

of the dialysis is performed at arterial-inflow rates of 250 to 350 ml. per minute. As in the standard method of dialysis, the plastic venous reservoir bag is occasionally checked to ensure fluidity of the blood.

TABLE 2. *Results of Protamine Titrations in a Nephrectomized Dog (May 25, 1956).*

	SYSTEMIC CIRCULATION *Arterial-cannula samples*							EXTRACORPOREAL CIRCUIT *Venous-cannula blood*						
Duration of Dialysis (min)	Protamine conc. micrograms/ml							Protamine conc. micrograms/ml						
	0	5	10	15	20	50	100	0	5	10	15	20	50	100
5	−	+	+	+	+	+	+	−	−	−	−	−	−	+
27	+	+	+	+	+	+	+	30	−	−	−	−	−	−	+
67	+	+	+	+	+	+	+	72	−	−	−	−	−	−	+
95	+	+	+	+	+	+	+	102	−	−	−	−	−	+	+
120	+	+	+	+	+	+	+	122	−	−	−	−	−	+	+
145	+	+	+	+	+	+	+	147	−	−	−	−	−	+	+

+ − Clot at 15 min.
− − No clot at 15 min.

Beginning ten minutes after the start of dialysis, heparin-protamine titrations are performed approximately every fifteen minutes during the first hour and less frequently thereafter, depending upon the smoothness of the control achieved. The rates of heparin and protamine delivered are varied according to the results of the titrations. Both arterial-sample tubes should show a firm clot at fifteen minutes. The saline tube of the first arterial sample may not show a firm clot at fifteen minutes (Tables 1 and 2) because the heparin initially present in the venous and arterial cannulae has not been neutralized. Contrariwise, on the venous side, the row numbered 1 (containing only saline solution) should never show a clot at fifteen minutes, whereas in the tubes from row numbered 4 (containing 15 microgm. of protamine) clotting is expected. The rate of heparin-protamine inflow is adjusted so that, on the venous side, clotting occurs in fifteen minutes in the tubes of rows numbered 3 and 4, but fails to occur in those numbered 1 and 2. If clotting fails to occur in the tubes of rows numbered 3 and 4, one can lower the level of heparinization by slowing the Sigmamotor pump.

Since different lots of heparin and protamine may have different potencies, one may encounter either excess heparin or excess protamine effect. An excess heparin effect would be evident by the absence of clot formation at fifteen minutes in the rows numbered 1 and 2 of the arterial samples. The addition of more protamine to the protamine infusion bottle would correct this difficulty. On the other hand, clotting in the tubes of rows numbered 1 and 2 of the venous-return samples means either an inadequate level of heparinization (with a *correct* ratio of heparin to protamine) or protamine excess (*incorrect* ratio of heparin to protamine). The former alternative is easily and rapidly corrected by an increase in the rate of the Sigmamotor pump; the latter requires an increase in the concentration of the heparin infusion, as pointed out below in the discussion.

At the completion of dialysis, the two catheters that pass through the Sigmamotor pump are rinsed and immersed in aqueous Zephiran (1:1000) for at least twenty-four hours. Before being used again the catheters are thoroughly rinsed with 5 per cent dextrose in water. All other tubing is discarded.

RESULTS

The procedure was initially tested and modified with the use of a dog weighing 32 kg. as a subject. Two days after bilateral nephrectomy, the dog was anesthetized with pentobarbital sodium, and hemodialysis was performed for a period of two and a half hours (Table 2). The total heparin dose used was 7.5 mg. per kilogram of body weight, and the total protamine dose 9.0 mg. per kilogram. Inspection of the data reveals that, after the first sample, blood removed from the systemic circulation showed no heparin effect, whereas at the same time there was marked heparinization in the extracorporeal circuit. In fact, inspection of the venous-sample data reveals that quantities of heparin far in excess of those actually needed were used.

After dialysis the dog did fairly well for the next three days. On the fourth day, as part of another study, he received a renal homotransplant into the neck. After this procedure, which failed technically, the dog succumbed on the fifth post-dialysis day. With this experience, the technic was used on 2 human patients.

CASE 1. L. R. (S.U.H. 353207), a 17-year-old girl, entered Stanford University Hospitals on May 31, 1956, with nausea, vomiting, anemia, lethargy, an episode of hematemesis and possible melena, and a weight loss of 6.8 kg. (15 pounds) after what was apparently a typical attack of mumps 7 weeks previously.

The blood pressure was 145/100. Except for pallor, minimal epigastric tenderness and minimal periorbital edema, there were no positive physical findings.

Laboratory investigations revealed a hematocrit of 27 per cent. Several urinalyses showed specific gravities of 1.010 and + + + tests for protein; the sediments contained numerous red blood cells, white blood cells and occasional granular casts per high-power field. No red-cell casts were seen. A urine culture revealed abundant growth of nonhemolytic streptococci. The serum creatinine was 17 mg., the serum urea 360 mg., the serum phosphorus 11.4 mg., and the serum calcium 8.5 mg. per 100 ml. The clotting time (Lee–White method) was 11.5 minutes. The bleeding time on 2 occasions was greater than 13 minutes and greater than 22 minutes. The stools were guaiac negative.

In the hospital the urinary output averaged 300 to 400 ml. per day. Vomiting persisted, lethargy increased, and the serum creatinine rose to 19.5 mg. per 100 ml. Renal biopsy by needle was deferred because of the prolonged bleeding time. Artificial-kidney dialysis was performed on the 6th hospital day. The history of hematemesis and possible melena during the week before admission, combined with the finding of a prolonged bleeding time, made this patient a suitable candidate for the method of heparinization described.

Dialysis lasted for 6 hours. The total heparin dose was 16.7 mg., and the total protamine dose used was 20 mg. per kilogram of body weight. Adequate heparinization of the extracorporeal circuit was maintained throughout (Table 1), and at the same time adequate protamine neutralization of the systemic circulation was provided as defined above.

The clinical course during dialysis was not significantly different from that usually observed with the standard method. Neither bleeding nor oozing was observed at the cut-down site. During the 6-hour period serum creatinine values fell from 19.5 mg. to 5.8 mg. per 100 ml. On the day after dialysis the bleeding time was 8 minutes.

Because of increasing clinical and laboratory evidence of uremia, the absence of bleeding after the previous dialysis and the reduction of the bleeding time to nearly normal, a 2d dialysis was initiated on June 15, standard methods being used. During this dialysis oozing at the cut-down site was marked.

This patient died of intractable renal failure on July 4, 1956. Post-mortem examination revealed subacute glomerulonephritis. No unusual deposits or pathologic lesions were found that could be ascribed to the heparin and protamine infusions.

CASE 2. J. D. (S.U.H. E132493), a 63-year-old man, manifested acute renal failure on May 21, 1956, subsequent to profound shock that followed an episode of acute pancreatitis and Dilaudid administration. Artificial-kidney dialyses were performed on May 29 and June 4, the standard method of systemic heparinization being used. After the 2d hemodialysis, hematemesis and melena occurred, and the hematocrit dropped from 30 to 21 per cent. Hemodialysis was performed for the 3d time on June 12, 1956. We had originally planned to employ the method of regional heparinization. However, unexpected initial difficulty with the outflow through the arterial cannula forced us to begin dialysis under systemic heparinization. After this difficulty had been corrected, the systemic heparin effect was neutralized by the slow intravenous administration of protamine. The remaining 5 hours of hemodialysis were then performed, with the use of the method of regional heparinization. The patient tolerated the procedure well, and there was no evidence of hemorrhage after this hemodialysis.

DISCUSSION

The method of regional heparinization described, using simultaneous infusion with heparin and protamine, is feasible when applied to the extracorporeal circuit of an artificial kidney. Adequate heparinization of the blood flowing through the artificial kidney can be attained without appreciably altering the patient's clotting time. Since the method is simple to perform, requires little extra equipment and needs few additional skills, it seems justified to explore its use in situations in which actual or potential internal or gastrointestinal bleeding provides the only contraindication to the use of the artificial kidney.

Adaptation of a Sigmamotor pump to provide a simple, constant infusion pump for simultaneous infusion of heparin and protamine has greatly facilitated the administration of these solutions. The rates of flow are adjusted in accordance with the results of repeated protamine titration tests done by the simplified technic described. The goal, which is easily achieved, is to maintain the minimum level of heparinization that will prevent activation of clotting factors in the extracorporeal circuit. At the same time the protamine titration test should show that there is no heparin effect in the patient. The extracorporeal heparin level is adjusted so that the heparin in 1 ml. of blood is neutralized by 10 to 15 microgm. of protamine. One can raise or lower this concentration by adjusting the speed of the Sigmamotor pump. Needed changes in the rate of flow of protamine occur simultaneously and automatically.

The ratio of the concentrations of the heparin and protamine solutions used was established by prior experience in dogs (described in the first section of this report[2]). A large number of experiments, with several different lots of each solution (but from the same manufacturers), have borne out the validity of the ratio of 6 parts of protamine to 5 parts of heparin. However, we are aware of the fact that the potency of different lots of both heparin and protamine has been reported to vary considerably, and we are prepared to make adjustments if the results of the protamine titrations indicate that they are necessary. One reason why neutralization of the heparin has been easy to achieve is that there is a wide range of protamine concentrations that will restore the clotting time of a given sample of heparinized blood to normal.[7] We are using ratios that are close to the minimum needed doses of protamine, but the slight excess of protamine that is constantly being added may build up over a period of hours and neutralize the heparin being infused. This situation can be corrected by an increase in the heparin concentration in the infusion bottle (as discussed above under Materials and Methods).

Experience to date has been limited to 2 patients who were potential rather than active bleeders at the time of dialysis. Case 1 bled from the gastrointestinal tract during the week before dialysis. No bleeding occurred during or after dialysis by the technic described above, but marked oozing occurred at the operative site at the time of a subsequent dialysis using systemic heparinization. Case 2 had severe gastrointestinal bleeding after a previous dialysis by the standard technic. No bleeding was encountered when the extracorporeal circuit alone was heparinized. These results are encouraging but further studies will be necessary before one can say with confidence that this technic permits the use of an artificial kidney for a patient with an actively bleeding internal lesion.

SUMMARY

A method of artificial-kidney hemodialysis without systemic heparinization is described. It has been used in 2 patients.

The procedure is offered as an adjunct to the standard use of the artificial kidney in cases in which systemic heparinization might be hazardous.

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OBSERVATIONS IN A "CONTROL" GROUP OF PATIENTS IN PSYCHOSOMATIC INVESTIGATION*

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OVER a year ago we began a study concerning hyperthyroidism that included some inquiry into the sociologic and emotional characteristics of patients with this disorder. To provide a group for purposes of comparison — in effect a "control" group — we selected patients with infectious hepatitis for the following reasons: this is a disease of probable viral etiology, certainly not generally placed in the category of the "psychosomatic" illnesses; it occurs most commonly in young adults and is associated with a period of hospitalization comparable to that of our patients with hyperthyroidism; and infectious hepatitis is a disease bearing a good prognosis, engendering optimism on the part of the responsible physicians and nurses. This report is concerned with the observations in the patients with hepatitis — our "control" group.

METHODS

The subjects were 25 consecutive patients admitted to the Boston Veterans Administration Hospital with clinical evidence of infectious hepatitis and laboratory tests supporting the clinical impression. Only 2 patients were excluded from the study because the etiology of the acute liver disease had to be questioned in view of severe chronic alcoholism. None of the patients had received a transfusion in the six months before illness, although 3 had been given injections during that interval, and therefore could have had homologous serum hepatitis. The patients were told that we were conducting a research study of hepatitis and were interested in finding out as much as we could about people with the disease. All patients were interviewed by the same internist (S.P.) on at least two and usually three separate occasions. Each interview lasted approximately an hour, and was carried out in the room of the patient, who was encouraged to do most of the talking. In addition, most of the patients were seen independently by a psychiatric social worker (J.H.).

RESULTS

General Description

The age distribution (Table 1) reflected the prevalence of infectious hepatitis. The distribution according to sex, color, marital status and religion was consistent with that of the hospital as a whole.

Educational Level

Four of the 17 high-school graduates (Table 2) were pursuing further education at the time of illness, and 4 had attempted but discontinued such efforts in the past. All 5 who had completed only grammar school started high school but never completed the course. Twelve patients attended school while holding part-time or full-time jobs. Nine had failed to achieve their educational goals at the time of this study. Thus, educational disappointment was prevalent.

Occupation

It is seen in Table 3 that the group varied in occupation from unskilled laborers to professional people.§ Occupational adjustment was described as good in 10, fair in 5 and poor in 10 subjects.

Childhood Background

The group as a whole was derived from large families of low income with an appreciable number of "broken homes" (Table 4). Many patients occupied "special" positions in the sibling order.

Marital History

Of the 17 married subjects, 7 had serious marital problems (Table 5).

Emotional Status

Five patients had had a psychiatric consultation in the past (Table 6). Two more requested psychiatric help during the period of study. Of the 25 patients, 7 had emotional symptoms (depression, anxiety, fear, hypochondriasis, impulsiveness and submissiveness) that they considered to be of moderate severity and at least partially incapacitating. We considered 2 others to have serious emotional symptoms. Frank depressive symptoms were observed in 4 subjects, 3 of whom had had similar reactions to adversity in the past. Our patients varied widely in their personality structure, and no predominant type was discernible although 10 appeared, during the course of study, to have fairly prominent dependent traits.

Antecedent Emotional Experiences

Of great interest to us was the observation that 18 of our 25 patients had distinct histories of acutely

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§Nomenclature comparable to that used by the United States Bureau of Census.

disturbing emotional experiences that occurred four to nine weeks before the onset of hepatitis. Although these episodes frequently involved a variety of conflicts, the major nature of the incident is listed in Table 7.

A few examples may be recorded. One patient was suddenly confronted by the fact that his marriage was not a legal one. Another received anonymous telephone calls threatening him and his family during a heated labor dispute in which he was actively involved. Another patient's wife had a breast biopsy, followed the next day by a hysterectomy, both procedures associated with much fear of cancer. One patient separated from his wife in a dispute that involved police intervention. Another conscientious provider and chronic "worrier" lost his job shortly after having been reassured by his supervisor that the rumors of employee reduction were ill founded. Still another separated from his wife because he wanted a greater share of his salary for "spending money" — he returned home within a few days, considering it probably worse to live alone. In another case a patient's aunt, by whom he had been brought up, died six weeks before onset of the illness, and he was profoundly distressed by her death.

In 12 of the 18 acutely disturbing events that occurred shortly before the onset of illness, there was some element (threatened or actual) of separation from or loss of someone close. This involved the wife in 9, the mother (or aunt) in 2 and the father in 1.

TABLE 1. *General Descriptive Data.*

AGE RANGE	MALE PATIENTS	FEMALE PATIENTS	WHITE PATIENTS	NEGRO PATIENTS	ORIENTAL PATIENTS	MARRIED PATIENTS	CATHOLIC PATIENTS	PROTESTANT PATIENTS	JEWISH PATIENTS
yr.									
22-46*	24	1	22	2	1	17†	15	8	2

*Average, 31 yr.
†3 separated.

TABLE 2. *Educational Status.*

STATUS	NO. OF PATIENTS
College graduate	2
Nurses-training-school graduate	1
High-school graduate	17
Grammar-school graduate	5

Summary of Results in Hepatitis

Figure 1 demonstrates that this striking number of unfavorable environmental conditions and emotional difficulties involved most of the patients and did not represent a concentration of misfortune in a few people. The lightning depicts the acute episode before illness; the split head indicates severe emotional problems and history of psychiatric help or the request for such assistance; the unbroken heart refers to marriage, and the black, broken heart to serious marital discord; the broken foundation is the broken home. The first row across consists of patients with all these unhappy factors present, the next row 3 factors, the third row 2, and the fourth row 1, including 5 who revealed only external stress. Only the 3 patients in the last row seemed to have escaped completely, and they were single.

The Next Step

At this point in our investigation it became apparent that it was necessary to control our "control" group. We therefore studied 10 patients of the same age group with proved acute appendicitis and 10 with pneumonia. The observations concerning environmental circumstances and emotional features in these groups were in general quite comparable to those described in the patients with hepatitis. Some of these findings are listed in Table 8.

TABLE 3. *Occupational Status.*

OCCUPATION	NO. OF PATIENTS
Service	5
Craftsmen	5
Clerical & sales	3
Professional	3
Operatives	2
Manager	2
Laborers	2
Student	1
Apprentice	1
Unemployed laborer	1

DISCUSSION

Certainly, the patients described above constitute a troubled group, having had environmental handicaps, marital difficulties, occupational frustrations and important emotional symptoms. Others have reported similar observations not only in patients with so-called psychosomatic diseases but also in a variety of medical and surgical illnesses.[1-6] It is important that these other studies were carried out primarily in large general hospitals both here and abroad, suggesting that our control group is not unique when

compared with other reported hospitalized patients. Nevertheless, further studies are required to ascertain whether the population groups from which our patients are derived are remarkable for their incidence of sociologic and emotional difficulties. This general problem is discussed further below.

The observation of so many acute and grossly upsetting experiences before the onset of illness is of interest. Similar observations are reported in a variety of conditions, especially the traditional psychosomatic ones. Frequently, some role in causality is attributed to these disturbing events. Indeed, Halliday,[7] discussing the very concept of psychosomatic disease (and infectious diseases are here specifically excluded by the author), wrote:

> Controlled investigations of a series of unselected patients have been made in a number of affections including asthma, peptic ulcer, hypertension, mucous colitis, exophthalmic goiter, and rheumatoid arthritis; these indicate that in a significantly high proportion of cases the particular morbid process emerged, or recurred, when the patient met an emotionally upsetting external event or a period of abnormal stress. It may be inferred, therefore, that many of these persons would not have responded with their particular kind of morbid behavior — would not have taken ill when they did — in the absence of such events. In a minority no such dramatic events nor any undue stresses could be elicited from the history.

Dunbar,[8] on the other hand, states that too often an etiologic relation between a psychic difficulty and an illness has been assumed without proof. She goes on, however, to interpret these observations differently:

> Hence life charts indicating a relationship between such factors as unhappiness in the family and the onset of a specific organic illness may be misleading. Unhappiness in the family may be a precipitating factor in any illness and not specific for any given disease such for example, as arthritis.

Indeed, acute upsetting events occurring before illness have been noted in patients with appendicitis and pneumonia with causality attributed to these occurrences.[8-12] That the liver has been thought for many years to have a close relation to emotional phenomena is exemplified in both medical and lay literature by the use of the word "melancholia," which literally means "black bile." Johnson[13] wrote in 1820, "In health, it is well known that this organ [the liver] is greatly under the influence of the passions." Others have described jaundice, possibly hepatitis in some cases, as occurring after emotionally disturbing events.[8,14,15] The possible relation of biliary flow and liver-function tests to psychologic phenomena is adequately discussed elsewhere.[16-18] Depression is frequently mentioned in the literature as a symptom of hepatitis.[19-22] It is apparent from the original reports, however, that frank depression in hepatitis is actually uncommon (occurring in less than 3 per cent of the series of Findlay et al.[21]), although when present it is obviously an important and disturbing symptom (and perhaps for that reason has received considerable attention).

Previous reports as well as the present study indicate that acutely upsetting emotional experiences are common before the onset of a variety of illnesses. Observations such as these are subject to at least two general interpretations: emotional distress may

TABLE 4. *Data on Family Background.*

BACKGROUND		NO. OF PATIENTS
Broken home		9
By death of father	3	
By death of mother	1	
By separation	5	
Parent with alcoholism*		5
Mother dominant parental figure†		12
Father dominant parental figure†		3
"Poor" economic status‡		8
"Adequate" economic status§		14
"Comfortable" economic status¶		3
1-3 children in family		12
4 or more children in family		13
Patient oldest child in family		7
Patient youngest child in family		5
Patient youngest male child in family		5
Patient only child in family		1
Continued close family tie		15

*Father in all.
†Patient appraisal.
‡Necessities a problem.
§Only necessities available.
¶Some minor luxuries available.

TABLE 5. *Marital Status.*

STATUS	NO. OF PATIENTS
Married*	17
Separated at time of study	3
Formerly separated & reconciled	1
Previously divorced & remarried	2
Seriously contemplating separation at time of study	1
Parent of 3 or more children†	4
Parent of 2 children†	7
Parent of 1 child†	5
No children†	1

*Age married: 17-34 (average, 25) yr.
†Average, 2 (19 males, 15 females).

TABLE 6. *Emotional Status.*

STATUS	NO. OF PATIENTS
Previous psychiatric help	5
Requested psychiatric help	2
Major emotional symptoms	9
Frank depressive symptoms	4

be an important determinant of susceptibility to a variety of disorders; and such episodes may merely be part of the living process and represent occurrences that bear only a chance, temporal relation to the onset of organic illness. There is indeed a vast literature describing observations of different varieties concerned with the possible role of emotional phenomena in determining "resistance" to disease.[8,16,23-27] Moreover, certain people without apparent somatic defects are alleged to be more readily afflicted with illness than others.[28] It has also been suggested that patients with neurosis have more somatic disease than control subjects.[29] It is of interest that, in the same study, patients with neurosis did not have a higher prevalence of hepatitis, appendicitis or pneumonia than the control groups although the total occurrence of somatic disease was apparently higher than in the control group.[29] In recent years the autonomic nervous system and the adrenal glands have been considered possible routes by which psychic phenomena may influence susceptibility and resistance.[24,30] It is our opinion that although the present state of knowledge allows for the possibility that psychologic disturbances affect resistance to disease, the proof of such a relation is not established.

TABLE 7. *Disturbing Emotional Experiences.*

EXPERIENCE	NO. OF PATIENTS
Marital discord	4
Financial difficulty	4
Employment (or school) problem	6
Serious illness in family	3
Acute anxiety reaction	1

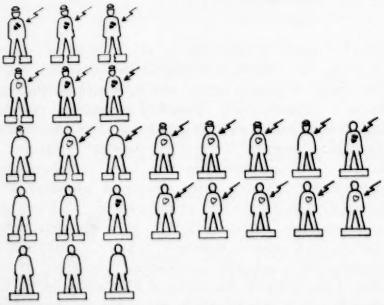

FIGURE 1. *Summary of Unfavorable Environmental Conditions (the Various Symbols Are Explained in the Text).*

Organically healthy subjects have received some attention in the literature. In general they have been found to have a significant number of emotional disturbances although somewhat fewer than patients hospitalized with organic disease.[2,3,31] Such observations may be interpreted in many ways, including the possibility that the sick person is more introspective, more concerned with causality and more interested in discussing his problems than his healthy neighbor. It was certainly common for our patients to relate their illness to a "rundown condition brought on by worry."

TABLE 8. *Environmental and Emotional Factors in the Control Group.*

FACTOR	10 PATIENTS WITH APPENDICITIS	10 PATIENTS WITH PNEUMONIA
	NUMBER	NUMBER
Broken home	2	4
Marital discord	2	3
Psychiatric help	1	2
"Serious" emotional symptoms	3	4
Recent distressing episodes	4	6
Separation (threatened or actual)	4	4

The entire problem of the "controlled" study in psychosomatic investigation is both difficult and important. It is actually a dual one in that a test patient group may be compared with a "normal" group as well as with other members of the same patient population. Although the information derived from the study of both varieties of control groups is important, it is apparent that the study of "normal subjects" presents great obstacles.[32,33] These are the obvious difficulties involved in the selection of a "normal" control group, and, as indicated above, even if such a group is selected, the information obtained from a "healthy" volunteer need not be comparable to the data derived from the same person during illness. Statistics on the general population have been used as "control" data, but this method has the serious limitation of including groups that do not contribute to the particular patient population under special consideration. On the other hand the study of other groups of patients drawn from the same general patient population provides a more relevant control sample for observations under conditions of illness and hospitalization.[32] Thus, such a control study makes it possible to test the hypothesis relating specific personality types to individual psychosomatic diseases and also provides the investigator with the opportunity to determine if the stress preceding the psychosomatic disease is unique either in its nature or in the patient's reaction to it. The very diverse natures of the disturbing experiences before the onset of hepatitis in a group with varied personality structure seem to offer ample opportunity for the establishment of unique characteristics in personality and stress in comparable test groups.

The difficulty of selection of a valid control group is apparent. Moreover, the question of whether the use of controls as employed in other biologic sciences is at all applicable to psychiatric studies has been raised. There are those who hold that causal relations can be defined only by technics considered to allow for the detailed interpretation of such relations in each particular case, and others who believe that analytic methodology does allow for a system of controls.[34] Whitehorn and Zilboorg,[35] considering the problems of psychiatric research in 1933, wrote as follows:

> One may mention in this connection that a certain tradition in psychiatric work also impairs the scientific clarity of our research. In chemistry, biology and in medical science we always use parallel observations, called "controls" and these provide a basis for comparison as well as a check on the purity of the experiment. Psychiatric research workers, even those of the highest type, frequently fail to follow this laudable method of "normal controls."

The same authors, noting a specific study for its lack of control observations, stated, ". . . without such a study we are bound to remain in the realm of impressionistic psychiatry." Finally, Groen,[36] in 1950, made the following observation:

> Truly just a description of personality traits and conflict situations in certain diseases is not enough to draw conclusions about the existence and nature of psychosomatic relationships in various diseases. The formulation of such a relationship must be supplemented by experimental, reproducible evidence before it can graduate from an indication to a proof. But the careful taking of a history and the assiduous clinical observation of a patient's behavior in various situations should never be forgotten or despised.

Summary and Conclusions

Twenty-five patients with infectious hepatitis were selected as a control group in the course of psychosomatic investigation. Subsequently, 10 patients with pneumonia and ten with acute appendicitis were also studied. These patients had a variety of social difficulties and emotional problems similar to those described in many psychosomatic illnesses. A history of an acute emotional upset in the recent premorbid period was commonly elicited.

The mere presence of environmental handicaps, emotional problems and antecedent distressing emotional experiences in any patient group cannot be considered evidence or proof that these factors necessarily bear any etiologic relation to a pathologic state. On the other hand this study does not exclude the possibility of such a causal relation, the proof of which would have to be sought by other means.

In the study of sociologic and emotional aspects of psychosomatic disease it is considered essential to have control observations on an entirely comparable patient population for the significance of the findings to be interpreted in any test group.

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RELATION OF THYROID ENLARGEMENT TO TRACHEAL CONFIGURATION*

An Anatomicoroentgenologic Correlation

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THE significance of the discrete thyroid nodule in relation to tracheal configuration is one aspect of a study of thyroid adenomas that has been undertaken at Montefiore Hospital. We have collected 15 cases in which operation was carried out by several different surgeons at this hospital because of solitary thyroid nodules. In this group routine roentgenograms of the chest taken before operation were reviewed to correlate the size of the unilateral thyroid mass with the degree of impression and distortion of the tracheal air column. Two additional cases were seen with autopsy correlation of thyroid mass and change in the tracheal air column.

The descriptions of the anatomy of the trachea vary widely, depending on the source of the data. The point of origin of the trachea is relatively fixed. The trachea begins at the cricoid cartilage at the level of the lower border of the sixth cervical vertebra, follows a completely mid-line course as it descends through the neck and superior mediastinum, deviates slightly to the right to make room for the

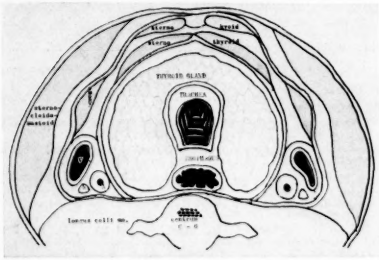

FIGURE 1. *Anatomic Cross-section through the Neck at the Sixth Cervical Vertebra (Schematic).*

arch of the aorta and ends its bifurcation into the right and left main bronchi. The width of the tracheal lumen in the sagittal projection is given at 16.5 mm. in adults.[1] Measurements on roentgenograms show a considerably wider variation in size, ranging from 15 to over 22 mm. This apparent discrepancy is easily explained by the difference between the dynamic diameter of the trachea in vivo compared with that in the post-mortem specimen. There is also a distortion factor in the roentgenogram. The level of the bifurcation of the trachea is subject to even wider variations. Anatomically, this level has been established at the upper border of the fifth thoracic vertebra. Our own measurements agree with those of Meschan,[2] who places the level at anywhere from the fifth to the eighth thoracic vertebra. There are three explanations for this wide variation between cadaver and the roentgenogram of the chest:

Roentgenograms of the chest are exposed with the patient in deep inspiration. Macklin[3] has shown by superimposing inspiration-expiration films of the chest that the level of the bifurcation of the trachea descends with inspiration.

The post-mortem examination is done in the recumbent posture as compared with the erect position for the roentgenogram. Here, again, Lachman[4] has shown that there is a definite gravitational descent of all the organs in the erect position, with the tracheal bifurcation participating in this process.

Roentgenographic distortion modifies the exact site of bifurcation.

The trachea pursues an exact mid-line course in the neck. Because of this course, even subtle deviations from the normal are definitely indicative of space-occupying lesions in the lateral neck structures.

TABLE 1. *Tracheal Configuration and Diagnosis in 17 Cases.*

CASE NO.	AGE	SEX	DIAGNOSIS	DIMENSIONS OF MASS	VOLUME*	TRACHEAL DEVIATION†
	yr.			cm.	ml.	
1	45	F	Adenoma	1 x 2.5 x 3	7.5	0
2	18	F	Anaplastic carcinoma	2.4 x 2.4 x 2.4	13.8	0
3	48	F	Adenocarcinoma	2 x 2.5 x 3	15	+
4	28	F	Adenoma	2.5 x 2.5 x 2.5	15.6	+
5	39	M	Adenoma	3 x 3 x 3	27	+
6	63	F	Carcinoma	3.5 x 3.5 x 3.5	42.9	+
7	52	M	Adenoma	3.5 x 3.5 x 3.5	42.9	+ to ++
8	47	F	Lymphosarcoma	3.5 x 3.5 x 3.5	42.9	++
9	33	F	Carcinoma	3 x 4 x 6	72	++
10	52	M	Carcinoma	4 x 4.5 x 5.5	99	+++
11	65	F	Adenoma	7 x 4 x 4	112	+++
12	47	F	Adenoma	5 x 5 x 5	125	+++
13	54	F	Adenoma	5 x 5 x 5	125	+++
14	45	M	Adenoma	8 x 5 x 4	160	+++
15	58	F	Adenoma	4 x 5.5 x 8	176	+++
16	50	F	Adenoma	5 x 6.5 x 5.7	185	+++
17	45	F	Adenoma	14 x 10 x 9	1260	+++

*Volume for practical purposes represents length x width x height.

†Tracheal deviation: + = indented homolateral wall; ++ = indented homolateral wall up to mid-line; +++ = indented homolateral wall across mid-line.

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The thyroid gland is relatively confined within its fossa. The gland is intimately in contact with the external carotid artery and the internal jugular vein. Each lobe is attached not only by the isthmus but also by the investure of the lateral expansion of the pretracheal division of the deep cervical fascia. This anatomic situation places the thyroid gland in intimate relation to the trachea. Furthermore, for practical purposes, the actual volumetric capacity of the infrahyoid cervical area is relatively limited as far as the expansion of solid viscera is concerned. The area is bounded laterally by the sternocleidomastoid and anteriorly by the strap muscles. The attachment of the sternothyroid to the oblique line of the thyroid cartilage limits superior extension. Unilateral thyroid enlargement may displace the carotid sheath laterally or attenuate the strap muscles so as to produce an anterior prominence. However, alterations in positional relations are first reflected within the confines of the relatively closed space and are seen roentgenographically as alterations in the tracheal air column (Fig. 1).

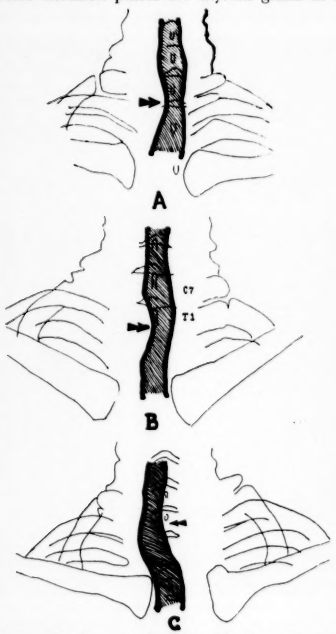

FIGURE 2. *Tracings of the Thyroid Area As Seen in Roentgenograms of the Chest in Actual Cases.*

A=*tracheal-wall indentation (+) due to a thyroid mass on the right.*

B=*tracheal-wall indentation on reaching to the mid-line (++) and due to a thyroid tumor on the right, with convex bowing of the contralateral tracheal wall.*

C=*tracheal-wall indentation extending beyond the mid-line (+++) and due to a thyroid mass on the left, with considerable convex bowing of the contralateral tracheal wall.*

In this study, multinodular goiters compressing both tracheal walls are not considered. The unilateral solitary adenomas were measured within the resected lobectomy specimen, which was fresh and unfixed. The size and weight of the surrounding normal thyroid parenchyma are not included.

CLINICAL MATERIAL

Table 1 lists the cases under consideration, 15 being postoperative and 2 post-mortem (Cases 3 and 8) correlations.

Tracheal deviation produced was considered + when the homolateral tracheal wall was merely indented, ++ when the indented homolateral wall reached the mid-line and +++ when the tracheal indentation extended beyond mid-line (Fig. 2*A*, *B* and *C*). The degree of shift was correlated with the volumetric size of the nodule. This dimension was obtained by multiplication of the three measured diameters of the adenoma (not strictly accurate

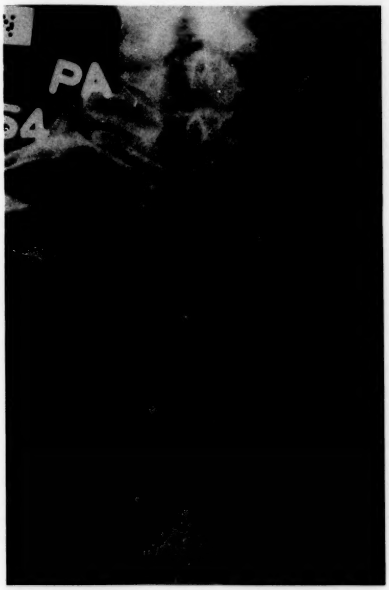

FIGURE 3. *Posteroanterior Roentgenogram of the Neck and Upper Chest in Case 1, Showing the Trachea in the Mid-line.*

The volume of the thyroid adenoma — 7.5 ml. — was well below the critical volume of 15 ml.

because the adenoma is really an ellipsoid, but we believe that this is more practical and reasonably accurate). No tracheal shift was observed in patients having volumes of less than 15 ml. A minimum volume of 100 ml. was required to produce a +++ deviation. In 6 of the 17 cases malignant nodules were found. Figures 3, 4 and 5 present examples, respectively, of no tracheal deviation, + to ++ deviation and +++ deviation in cases of thyroid mass.

The volume-shift correlation is consistent for this series and forms a preliminary basis for our study of such relations. It is probable that tracheal configurations are related to the direction of the long axis of the nodule. A nodule situated with its largest diameter in a vertical direction will not produce the same changes as a similar-sized nodule with its long axis placed horizontally. It is possible that long-standing, large, discrete adenomas grow vertically because of the vertical axis of the trachea and esophagus and the molding influence exerted by the mechanism of swallowing.

FIGURE 4. *Posteroanterior Roentgenogram in Case 7, Demonstrating Indentation on the Tracheal Wall by a Right-Sided Thyroid Adenoma, with Indentation Almost to the Mid-line (Considered + to ++). The volume of the adenoma was 32.9 ml.*

The degree of tracheal shift is unrelated to the histologic morphology of the thyroid nodule. In our series of 6 cases of thyroid cancer 4 caused significant deviation. Thus, we are unable to confirm Ritvo's[5] statement that "carcinoma of the thyroid tends to infiltrate the trachea, preventing the lateral displacement usually found in benign tumors. Hence, a mass in the thyroid without tracheal deviation is apt to be malignant." Our own observation from this small series is that benign and malignant tumors of the thyroid gland have an effect upon the tracheal wall solely because of their volume and that x-ray study is therefore of little value in differentiating histologic patterns.

FIGURE 5. *Posteroanterior Roentgenogram in Case 15, Giving an Example of +++ Tracheal Deviation Caused by a Large Left-Sided Thyroid Adenoma with a Volume of 176 Ml.*

Wichman and Schmidt[6] found that the trachea shifts toward a normal position after the removal of matching thyroid enlargements. In the 3 cases in which we were able to obtain follow-up roentgenograms after removal of a solitary adenoma, there was no reversal of the tracheal shift.

If our conclusions prove valid for a larger series of cases, the changes in tracheal air column as seen in the roentgenogram of the chest present a graphic and accurate method of evaluating the size of thyroid tumors.

SUMMARY

The volumetric capacity of the infracricoid area is relatively limited.

Unilateral thyroid adenomas produce alterations in tracheal configurations that are related to the

volume of the adenoma. The tracheal wall is initially indented unilaterally and then shifted across the midline. A minimum volume of 15 ml. is required to produce a + change. All volumes over 100 ml. cause a shift of the homolateral wall across the mid-line.

The roentgenogram of the chest is of no value in the differentiation of benign and malignant thyroid tumors, as far as change in the tracheal air column alone is concerned.

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SOME PREOPERATIVE WARNINGS OF POTENTIAL OPERATING-ROOM DEATHS*

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PHILADELPHIA

CAREFUL study of the circumstances surrounding the deaths of surgical patients has proved profitable in defining groups of patients who are candidates for catastrophe in the operating room or in the immediate postoperative period. Many of the hazards involved are generally recognized and understood. Others may be apparent if the anesthetist, surgeon or internist studies the problem before operation. In a final group the mechanism of the complication is obscure, and forewarning comes only from previous experience. It is the purpose of this report to attempt to classify these hazards and to relate certain experiences encountered by the anesthesia service of a large university hospital over the period of the last ten years, during which approximately 150,000 anesthetics have been administered.

Hazards Produced by Improper Preparation of Patients for Anesthesia and Operation

Most of the hazards in this group can be avoided by careful preparation of the patient for operation. Unfortunately, however, in the rush of modern surgical practice, the potential danger may be overlooked for the personal convenience of the surgical and anesthetic attendants under the guise of surgical expediency.

Presence of Food in the Stomach

Although the danger of vomiting during or immediately after anesthesia is common knowledge, deaths from aspiration of vomitus are reported with discouraging regularity. The proper interval between the ingestion of food and anesthetization is usually placed at four or five hours. However, no fixed interval can be accepted. Emotion, apprehension and injury can delay gastric emptying for many hours. During the war an injured soldier was encountered who died during operation from aspiration of chunks of meat ingested twelve hours previously, before a relatively minor peripheral injury.

Involuntary vomiting may not be the sole factor leading to aspiration. A death from aspiration of stomach contents occurred when a surgeon manually collapsed a distended stomach during an exploratory laparotomy under general anesthesia. We have also observed pneumonia that followed aspiration of gastric fluid forced into the pharynx by external abdominal pressure by one surgeon during pelvic examination of the patient by another.

Patients often unwittingly expose themselves to this hazard by failing to follow instructions or, what is more important, when the instructions given the patient by his physician have not been sufficiently explicit. This occurs most commonly in patients admitted to the hospital on the day of operation. Instructions should be detailed and preferably written to avoid confusion.

If general anesthesia is imperative, in the presence of a full stomach the patient's stomach should be emptied, preferably by induced vomiting before the administration of preanesthetic medication. A Levin tube is inadequate for removal of gastric contents except that its attempted introduction often causes the patient to vomit. When vomiting cannot be induced, the operation or delivery should be performed, if possible, with local or regional block anesthesia. If general anesthesia is mandatory, it may first be necessary to insert a cuffed endotracheal tube, using topical anesthesia. It is well to recall, however, that conscious patients can also aspirate stomach contents; therefore, spinal anesthesia is not the whole answer to anesthesia for patients with full stomachs. One of the most common emergency surgical conditions in which the recent ingestion of food is encountered is fracture in children. There appears little reason to risk general anesthesia in such situations unless the circulation has been compromised. It is safer to delay reduction of the fracture for eight to twelve hours.

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Apprehension

The markedly apprehensive patient is a potential candidate for death in the operating room. At least four times in the past ten years we have had patients who died during or immediately after operation, having evinced marked preoperative apprehension. In 2 cases it was believed that the patient's apprehension was in part due to inadequate preoperative discussion with his physicians. In the others apprehension persisted despite discussion.

The relation of apprehension to death is obscure. None of these patients were classified as being poor surgical risks. By ordinary standards none should have died. Their mechanism of death followed no single pattern. The influence of endogenously released epinephrine under the stress of anesthesia and operation can only be speculative. Regardless of mechanics it is obvious that special attention must be given the apprehensive patient. The reasons for operation must be thoroughly discussed, and judicious sedation must be employed preoperatively. The statement by a patient that he is going to die should give rise to concern among his physicians.

Hypovolemia

It is generally recognized that patients with certain syndromes and those who are inactive or bed ridden may have a reduction in blood volume. Ordinarily, this may be of little concern to the patient, but when he is faced with the stress of a major surgical procedure, it may be of real significance to his physicians. The anesthetized hypovolemic patient has a diminished circulatory reserve; he may be unable to compensate for the depressant effects of anesthetic agents or adjuncts; he may be intolerant to changes in body position; and he may demonstrate sudden and alarming hypotension in response to relatively minor blood loss. He is especially unable to compensate for major hemorrhage.

We have been particularly watchful for hypovolemia in the following situations: patients with neoplastic or ulcerative lesions of the large bowel; those who have been bed ridden or in body casts for long periods; elderly persons who have led a sedentary existence; patients who have had extensive fluid loss for any reason; and those who have had multiple operations. Obviously, it is not practical to transfuse to a theoretical average normal all patients with blood-volume deficiencies. However, if a deficit of as much as 1500 to 2000 ml. exists, it is advisable to administer 500 to 1000 ml. of blood before operation. Awareness of the deficiency enables one to anticipate and prevent trouble. Once hypotension develops in the hypovolemic patient, a greater volume of blood is required to treat it than if hypotension were avoided.

Fever and Dehydration

The anesthetization of a febrile, dehydrated child is fraught with danger, and yet anesthetists are often called upon to administer anesthetics under these circumstances. Fever, dehydration, general anesthesia and carbon dioxide accumulation form a combination of factors that predispose to convulsions.[1] Consequently, anesthesia should be delayed when the first two signs exist. It is relatively simple to treat dehydration with intravenous infusion of fluids, and as a consequence the temperature is usually reduced. In spite of this, an unnecessary and hazardous "rush" label is frequently attached to these patients. They are often taken directly from receiving ward to operating room without benefit of fluids or sedatives. This is an invitation to disaster.

A 10-year-old boy was admitted to a small general hospital late in the evening. He was complaining of abdominal pain, had been vomiting intermittently for 20 hours, and was obviously dehydrated; the temperature was 101.6°F. by rectum, and the white-cell count was 15,000. A diagnosis of a ruptured appendix was made. The patient was taken directly to the operating room, where he was anesthetized with Vinethene and ether by the open-drop method. Twenty minutes later, as a gangrenous appendix was being removed, he began to have convulsions and became cyanotic. An attempt to start an intravenous infusion of fluids was unsuccessful because of the violent convulsions. Efforts were made to inject a barbiturate intravenously; the cyanosis deepened, the convulsions diminished, the heart ceased to beat, and the patient was pronounced dead.

Excluding hemorrhage or respiratory obstruction, there are few pressing indications for immediate operation. In the presence of fever and dehydration, operation is rarely urgent. It is far safer to spend an hour or two hydrating and preparing the patient for operation than to risk convulsions.

Preoperative Drug Therapy

The last decade has introduced a new and insidious hazard to many patients undergoing anesthesia and surgery. This is the multitude of drugs that patients are receiving daily and for long periods for a variety of real or fancied reasons. Thus, one is faced with patients who have for months or years received daily quotas of cortisone, chlorpromazine, promethazine, reserpine or one of the less potent tranquilizing drugs. The hazard lies in the fact that these drugs all appear directly or indirectly to affect the circulation when the patient is subjected to the stress of anesthesia and operation. The mechanisms are not completely understood, but the end result has been observed so commonly that the hazard is apparent.

Cortisone. Patients who have been treated with cortisone for long periods should continue to receive the drug before and throughout the surgical experience.[2,3] Removal of cortisone before operation may leave the patient in a state of relative adrenal exhaustion and therefore deny him the compensatory circulatory control so necessary during the period of surgical and anesthetic stress. The cortisone should be maintained or increased before and after operation. If a reduction in blood pressure occurs during

or after operation, it must be treated with hydrocortisone intravenously, vasopressor drugs and blood. However, since hypotension my be precipitous and prolonged, failure to be alerted to the possibilities of the situation may result in catastrophe.

Reserpine. Severe hypotension likewise may be seen in patients subjected to anesthesia and operation after having received long courses of reserpine.[4] The effects of this drug may persist for about ten days after it has been stopped. Hypotension may occur shortly after the induction of anesthesia, or it may be delayed. It may persist for days postoperatively, requiring support with intravenous administration of vasopressor drugs. The following case represents one of the most recent experiences with this phenomenon.

A 73-year-old woman was admitted to the hospital with the history and physical findings of an incarcerated inguinal hernia. She had been known to have hypertension for 2 years and had been taking 0.25 mg. of reserpine daily for that period. The blood pressure on admission was 190/100. One hour and thirty minutes later she was given 15 mg. of methoxamine intramuscularly, followed by spinal anesthesia with Pontocaine and glucose. A sensory level of anesthesia to the 4th thoracic dermatome was obtained. The blood pressure was maintained at 140/80 for 45 minutes, when it declined to 110/60. Phenylephrine (0.1 mg.) was injected intravenously, and the blood pressure returned to its previous level. In 25 minutes phenylephrine was again required. A large inguinal hernia was repaired during this period.

Postoperatively, the blood pressure remained at about 140/80 for 3 hours, and then suddenly fell to 85 systolic. Methoxamine was administered intramuscularly twice in 4 hours, after which an intravenous drip of nor-epinephrine was started, to maintain the systolic blood pressure at or above 110. This was continued for 48 hours. Methoxamine, 20 mg. intramuscularly, was then required at intervals of 3 or 4 hours for 3 days to keep the systolic blood pressure at about 110. On the 6th postoperative day, methoxamine was administered at intervals of 4 to 6 hours and on the 7th day vasopressor therapy was discontinued when the blood pressure stabilized at about 115/80 to 120/80. During the period of hypotension the pulse rate was consistently about 60, and did not increase in response to intravenous administration of atropine.

The etiology of the aforementioned hypotension has not been elucidated. Nevertheless, the danger is real and of grave concern. We have adopted the policy of withholding reserpine for a period of eight to ten days before performing elective surgery. Data are required on this interesting phenomenon.

Chlorpromazine and promethazine. The fact that chlorpromazine or promethazine predisposes to hypotension can easily be demonstrated. A high percentage of normal subjects to whom either of these drugs was administered parenterally fainted shortly after being tilted 60° in the head-up position.[5] In my experience the blood pressure of several anesthetized patients previously treated with chlorpromazine has disappeared when their body position was changed on the operating table. The great danger with both drugs appears to be their influence in dampening or abolishing reflex control of the circulation.

It should be obvious from the foregoing paragraphs that it is of the utmost importance for the anesthetist to be aware of the medication patients are taking. I have often found patients who have been routinely taking antihypertensive or tranquilizing drugs, and yet the fact has not appeared on their records. It has become increasingly important to inquire into the drug habits of patients.

Failure to Alert the Anesthesiologist to Previous Anesthetic Difficulties

Occasionally, a patient encounters serious circulatory or respiratory complications during the administration of an anesthetic, and as a consequence the operation must be postponed, curtailed or hurriedly completed. Under these circumstances it may be necessary to reoperate at a later date. When reoperation is planned, particularly if it is months or years later, it is important that the anesthetist know what the previous problems were. This is unnecessary when the same anesthesiologist is to administer the anesthetic, but it assumes supreme importance when there is to be a different anesthesiologist.

A 63-year-old woman was scheduled for a sigmoid colectomy for carcinoma. The only complicating factors were diabetes and a blood-volume deficit of 1000 ml. Anesthesia was maintained with cyclopropane and ether. Although the induction was smooth, the blood pressure promptly rose from a normal of 130/70 to range between 180/100 and 200/100 during the 1st hour of operation, and the pulse gradually increased to 160 per minute. This was accompanied by peripheral cyanosis despite adequate ventilation. The sigmoid colon was removed, but anastomosis was deferred because of the patient's condition. A colostomy was performed.

Postoperatively, the pulse, blood pressure and color gradually returned to normal over the period of 24 hours, and the remainder of the convalescence was without incident. Ten months later the patient returned for closure of the colostomy. The anesthesia department was not alerted to the patient's previous experience. A different anesthesiologist was assigned. He visited the patient preoperatively, but unfortunately she knew nothing of her previous difficulty and there was no mention of it on the chart. He failed to seek out the old record. She was again anesthetized with cyclopropane and ether. The same sequence of events occurred, with the addition of pulmonary edema. This time the postoperative course was stormy, with continued tachycardia, hypertension, and cyanosis. Forty hours after operation she suddenly died. At autopsy a pheochromocytoma was found.

Ether probably was a poor choice of agent. The catastrophe might have been avoided if the surgeon or internist had warned the anesthetist of the previous problem, or if the anesthetist had taken the time to examine the old record.

Hazards Produced by Pre-existing Disease Unrelated to Contemplated Surgery

All patients with symptoms referable to the heart should have a thorough cardiovascular examination before operation. This is important not only to detect cardiovascular disease but also to establish a base line for comparison if cardiovascular complications arise during or after operation. Patients commonly appear in the physician's office with no unusual divergence from their normal routine in sight and yet requesting routine physical examination. A surgical operation with its attendant anesthesia comprises

a significant stress, possibly one of the most severe stress situations a person of forty years of age or older may be called upon to face. Is it not reasonable, therefore, that such stress should be preceded by a careful examination of the body system most influenced by stress—namely, the cardiovascular system?

Angina Pectoris with or without Myocardial Infarction

Probably the leading cause of unexpected catastrophe in the operating room or in the immediate postoperative period is coronary-artery disease. Patients with such disease may suffer myocardial infarction or sudden death at any time and under any circumstance. They likewise may die suddenly before, during or after anesthesia and surgery no matter how skillfully the anesthetic was administered nor how minor the operation performed. Such patients have died during the night before scheduled operation, the morning of operation in the operating room while awaiting anesthesia, during operation, immediately after operation and during the first and second postoperative days when convalescence appeared to be progressing satisfactorily. Interestingly enough, patients with angina pectoris and myocardial infarction about whom there has been great concern have withstood anesthesia and major surgery exceedingly well and yet have succumbed weeks later at home while sitting quietly in a chair.

Faced with such hazards, these patients should be managed with the utmost skill and best possible teamwork during the operation and afterward as well. Hypoxia, hypotension or overloaded circulation during or after anesthesia will increase the mortality in this group.

Cardiac Arrhythmias

Certain arrhythmias appear more significant than others to the anesthetist. One of the most important is that of complete heart block. It is well known that patients with this syndrome are subject to sudden cardiac arrest. That the same complication may occur during anesthesia and operation is borne out by study of a series of such patients at the Peter Bent Brigham Hospital.[6] In 1 patient with complete heart block cardiac arrest developed while a caudal anesthesia was being administered for surgical correction of an anal fissure; the chest was opened immediately, and the heart massaged, and the patient is alive and well today, three years after the incident. The fissure has healed in the interim.

Unexplained tachycardia is likewise cause for concern. Any patient appearing in the operating room with unexplained tachycardia should have his operation postponed until the cause of the tachycardia has been ascertained. In my experience apprehension is not the most common cause of rapid heart rate under these circumstances. Tachycardia has often been found to be due to previously unsuspected organic heart disease or low blood volume.

Heart Failure

Patients with obvious cardiac failure seldom arrive in the operating room without warning. However, it is possible for undetected cardiac failure to develop in patients scheduled for operation. Under these circumstances, the operation should be delayed until the situation is brought under control. Rapid digitalization before anesthesia is not recommended. In the following case cardiac failure developed in a patient who was digitalized rapidly.

A 79-year-old woman was admitted to the hospital with a fractured hip. She was arteriosclerotic. The blood pressure was 160/70, the pulse was regular at 100, she was dyspneic, and the blood urea nitrogen was 32 mg. per 100 ml. She had had a hemiplegia on the right 4 months previously, with nearly complete recovery. She was scheduled for operation 2 days after admission. Preoperative medication was atropine sulfate, 0.4 mg. hypodermically. In the operating room, she was observed to have a blood pressure of 160/70, an irregular pulse rate of 140, and rales at both lung bases. A cardiac consultation was advised by the anesthesiologist. The surgeon suggested intravenous digitalization and advised that the operation was urgent. Anesthesia was induced shortly thereafter with thiopental and nitrous oxide and oxygen. Seven minutes later 0.4 mg. of digitoxin diluted to 5.0 ml. was slowly administered by the surgeon. Five minutes later the patient vomited and apparently aspirated some of the vomitus. Otherwise, the 2-hour operative course was uneventful, but at the termination of the procedure it was apparent that she had had a cerebrovascular accident. She never regained consciousness and died on the 5th postoperative day.

Early operation on patients with fractured hip is mandatory. The consensus is that it should rarely be delayed more than forty-eight hours. The urgency is never so great, however, that a few hours cannot be taken to accomplish digitalization. In the case reported above, the operation should have been postponed while an attempt was made to bring the cardiac failure under control.

Chronic Respiratory Disease

Chronic respiratory diseases increase the hazard of anesthesia and operation. Pulmonary emphysema is among the most important because it makes administration of a general anesthetic more difficult owing to poor gas exchange and increased secretions. The principal problem, however, may arise in the postanesthetic period. Patients with emphysema have great difficulty in clearing their respiratory tracts of secretions, and atelectasis and pneumonia easily develop. If patients with emphysema require operation within the chest, pulmonary-function studies should be made to determine their pulmonary reserve. Despite satisfactory reports death from pulmonary insufficiency may occur because of the inability of the patient to keep his respiratory tract clear of secretions and simultaneously to maintain adequate pulmonary ventilation.

Bronchial asthma likewise complicates the administration of anesthesia. Thiopental, cyclopropane, morphine and curare are contraindicated because of the possibility of bronchospasm. Most patients who

are prone to severe asthmatic attacks will warn the anesthetist, but some do not. It is well, therefore, for the patient's physician to acquaint the anesthetist with the history. The chart should contain a complete account of the situation. Only one who has witnessed an episode of severe bronchospasm, with its attendant cyanosis, hypertension and tachycardia, can appreciate the potentialities of the situation. No physician associated with such patients should promise them they will be put to sleep with "a little Pentothal."

Patients with chronic respiratory obstruction often can compensate satisfactorily when awake or naturally asleep, but lose their compensation when anesthetized. Sudden complete respiratory obstruction under these conditions may be fatal. When the airway is encroached upon by masses about the mouth, pharynx, cervical or mediastinal areas, it is wisest to insert a noncollapsible endotracheal tube with the patient awake. Once this has been accomplished, the anesthesia presents no special problem. Sometimes, the insertion of a tube under these circumstances is not easy, but the anesthetist should never rely on his ability to insert an endotracheal tube after the patient is asleep. This may be even more difficult.

Anesthesiology has long ceased to be a technical service, doling out sleep to patients appearing in the operating room in a manner similar to that of pouring gasoline into an automobile by a service-station attendant. Surgical procedures have become increasingly complex, more definitive, of longer duration and of greater hazard to the patient. Surgeons are willing to operate upon patients at either extreme of life, upon patients in the poorest physical condition and even with small prospect for success. The willingness of surgeons to operate upon almost any patient is in great measure due to the improvement in anesthetists, anesthetics and technics. However, further improvement is necessary and desirable. Alerting the anesthetist to important facts in the patient's past medical history may be life saving. The anesthetist's own careful study of the patient and his history and physical findings may be vital. However, awareness by the surgeon, internist and general practitioner of the anesthetist's problems may do much to facilitate the patient's safe course through a surgical operation.

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SPECIAL ARTICLE

THE FULL TREATMENT*

A Modern View of the Relief of Symptoms

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NEW YORK CITY

IT would be best if I started with a plain statement on how I feel about the relief of symptoms. My opinion is that relieving distressing symptoms is an exceedingly important aspect of medical care, and that to ignore the reactions of the patient to distress is to deprive him of one of the achievements of modern medicine. Beyond this, I believe that relieving the symptom is not necessarily more simple than treating the cause of a precisely diagnosed disease — that it often presents even more complex problems in therapy. The use of drugs for the relief of symptoms is an entirely different matter from the use of drugs for the support of physiologic processes or for the eradication of the causes of disease, and should receive special consideration. Nor is a scientific approach to medicine in any way inconsistent with an active concern over symptoms. A conciliatory attitude toward symptoms need not decrease interest in diagnosis, pathology or specific therapy. Because he has penicillin and what it represents, the doctor should not forget that, in relieving symptoms and in providing rest, relief and reassurance, he may exert an indirect but nevertheless an additional beneficial contribution to the treatment of disease.

A large literature has already accumulated on the effects of stress on function and in the causation of disease. Not everyone agrees regarding its precise role in disease or which diseases it may cause or aggravate, but few repudiate the reality or the importance of immediate and long-term reactions and adaptive responses that individuals may make to stress. It seems only reasonable to assume that internal distress in the form of somatic discomfort — with the anxieties that it may arouse and the fear symbols it can evoke — is as potent a force as that

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created by external situations arising from cultural, circumstantial or psychologic difficulties. It is stated that "those who would deal with pain as therapists must concern themselves especially with reactions to pain," but there is no reason to believe that pain alone among the symptoms excites deleterious responses.

It is a lengthy and sometimes impractical, if not impossible, process to treat a life situation that causes stress and deleterious adaptive reactions; this is one of the unfortunate limitations of the psychotherapeutic approach to "diseases of adaptation." On the other hand it is often both feasible and realistic to alleviate the distress of symptoms whose effects may be equally threatening.

This is not the prevalent view today. For the most part, if the patient gets his relief it is likely to come indirectly. If his doctor has a purely organic approach, the emphasis will be placed on anatomic and physiologic disturbances, and all the other facets of the patient's complaints are disregarded as being "merely" psychogenic. If his physician has a strong psychosomatic bias, emphasis will be on the psychic background of the disturbance, and the anatomic and physiologic aspects may well be relegated to second place. But in either case, the first effort will be to establish the cause of the illness and after that to treat the disease by removing, correcting or revealing the cause. The relief of the symptom per se is given little thought.

The modern physician may even preserve the symptom, using it not only as a guide to diagnosis but also as a map of the course of the disease and an index to the response to therapy; he may be so respectful of it that he is unwilling to attack it directly. The patient is advised to keep the physician informed of the progress of the symptom. Of course, if the diagnosis turns out to be accurate and if all goes well and according to plan the symptom will be alleviated, but that was not an important consideration in the plan of treatment.

But the physician should not take refuge in a superior feeling that, in expressing greater concern for etiology than suffering, he is tackling the more difficult as well as the more basic problem, for it is not a fact that it is invariably easier to relieve than to cure; today, the reverse is often true. Once a disease is properly identified, the target for the attack is clear, and there are physical signs and laboratory data against which the course of the disease and the response to therapy may be checked on a relatively objective basis — fever, pulse, weight, blood pressure, blood counts, sedimentation rates, blood cultures and so on. No such objective data chart the course of the symptom. The only observer of the symptom may be the sufferer, an interested party whose estimates of the relief provided by symptomatic therapy are necessarily subjective. On the other hand an attempt to use objective guides as an index of the reactions to symptomatic therapy may be very deceptive. The use of the vaginal smear as a guide to the response of hot flashes to estrogenic therapy is an example; although the changes in the character of the vaginal smear can be objectively determined, only the patient can tell when she no longer suffers the flashes. Relief of the patient's complaint may precede or be delayed beyond the restoration of a normal vaginal epithelium, or it may not parallel the nature of the vaginal smear at all. The restoration of normal vaginal cellular characteristics by no means guarantees that the patient no longer suffers flashes, and it was for their relief that she came to the physician.

The Symptom Experience

Definition

It is generally accepted that complete knowledge of the phenomenology of disease is essential to its treatment. It is equally true that precise and effective treatment of the symptom requires an understanding of its phenomenology. For this, a broad view of the symptom is essential, and any definition that considers it, as the dictionary does, merely an "aid to diagnosis" is inadequate. The symptom might be usefully considered a disturbance in the normal balance between stimulus and response: a normal response to an abnormal stimulus, or an abnormal response to a normal stimulus. Normal reactions to normal stimulation do not constitute symptoms. The borderline is not sharp, and it is sometimes difficult for doctor as well as patient to distinguish between a normal reaction and a symptom. The stimuli that induce symptoms may be physical, physiologic or psychologic, or a combination of any such excitants in any proportion. Stimuli include infections, degenerative changes, chemical, physical and psychic trauma, anxieties, stress and cultural pressures. The response that causes a symptom may be anatomic, physiologic or psychologic, or a combination.

Threshold of Symptom Perception

Wolff has reported that, in cases of pain, a well defined threshold of perception exists that is influenced by distraction, suggestion and other psychic factors. There is no reason to believe that analogous thresholds of perception do not exist for other symptoms, even though their determination is more elusive; nor is there any reason to consider that such thresholds of appreciation may not be influenced, like the pain threshold, by psychic or environmental forces.

Quantitation of Symptoms

The intensity of a symptom is a matter of considerable importance, for it plays an essential part in determining the patient's functional and psychic reactions to it. For pain, units of severity have been established, but there are no such designations for

most symptoms. A patient with a severe pain may compare it with the pain of relatively well known severity such as childbirth, renal colic or toothache, but there is no comparable standard for such simple and common symptoms as cough, nausea, and dyspnea. The number of distressing experiences may be useful in indicating some aspects of severity, but does not indicate the severity of the attack itself. Thus, although a patient with diarrhea may report the number of movements, or a patient with bronchiectasis the number of coughing fits, these reports indicate only frequency, which is merely one element of quantitation.

Quality of the Symptom

The quality of the symptom is important to both diagnosis and relief, but is often difficult to express. This is not only a matter of vocabulary; there are no universally recognized ways of clearly describing the varying quality of many symptoms. Most patients can distinguish fairly readily between sharp, dull and aching pain, or between dry and productive cough; but in other symptoms, such as vertigo, differences in quality are elusive.

Site of the Symptom

The location of the symptom is also significant. It may be deep or superficial, visceral or somatic. It may be localized in a particular organ or well defined area, or it may travel. In the latter type it is essential to note the path of its movement, whether it is reproducible and whether it follows clear anatomic lines.

Timing of Symptoms

When a symptom appears is important, for it may point to important circumstantial, physiologic and psychologic connections between symptoms and their causes. It should therefore be noted whether they occur in the morning before work, during work, after work or after particular experiences. Pain in bed before arising, for example, may point to the effects of the bed itself or to the recumbent position, or it may indicate anxieties that develop when daytime distractions are removed, or anxieties related to anticipated, actual or absent sexual activities.

Precipitating Cause of Symptoms

The precipitating cause of symptoms often suggests both diagnosis and treatment — for example, if the patient coughs only when he lies down flat in bed, this suggests left-sided heart failure and a course of treatment.

Patient's Discovery of Measures That Provide Relief

Measures that the patient has discovered to relieve symptoms are of practical importance and may provide leads to effective therapy. The patient's own trial-and-error therapy is often far more extensive than either he or his physician dreams, and the patient himself may have discarded as useless some forms of therapy that the physician would be inclined to try. It is usually both wise and practical for the physician to attempt to make sense out of the patient's observations on the results of his own therapy, for, even though the patient cannot be considered an objective observer, he is the only — as well as the last — judge of when he suffers least from his symptoms.

Ceiling of Appreciation

If one estimates the intensity of the complaint, one is likely to find not only a threshold but also a ceiling of appreciation beyond which more intense stimulation fails to bring about further increase in the intensity of the particular form of distress. This ceiling is important in the treatment of complaints of great intensity, for at this level symptoms no longer indicate the intensity of the noxious stimuli or the intensity of therapy necessary to relieve the distress.

Threshold of Complaints

Each patient has his own complaint threshold, a breaking point not unlike the "misery threshold" mentioned more than fifty years ago by William James in *Varieties of Religious Experience*. Beyond this point, distress, or the appreciation of abnormal sensation or function, elicits some form of complaint. This is to be distinguished from a threshold of appreciation — the symptom threshold. The majority of patients appreciate symptoms before they call them to the physician's attention, but when varies greatly. There are patients who may complain in anticipation of symptoms and others who complain when they have no physiologic disturbances at all — as in hysteria. Some complain the moment they appreciate any deviation from their norm, and still others endure distress until it becomes so plain that outside pressures force them to seek relief.

Reactions to Symptoms

There are physiologic reasons for relieving symptoms. Symptoms may evoke adaptive reactions that do not operate effectively for purposes of defense. Usually, the result is reversible, but occasionally, if these reactions are uncontrolled, they may undermine vital functions to a degree that causes irreversible injury. Thus, pain may reduce renal function, and vomiting and diarrhea may cause serious electrolyte imbalance or dehydration.

When the symptom is viewed in this light, it attains a pernicious quality of its own and presents the therapist with a substantial and logical reason for its direct relief. Symptoms are not inert; they are alive, and each symptom has its own life process.

The Nature of Relief

Comfort is something everyone prizes; the evidence is everywhere, from foam-rubber mattresses, electric blankets, air conditioning and power-steering to peace of mind. Relief from distress is not only acceptable, per se, as part of the cult of comfort but also fundamental to modern concepts of disease and treatment.

Dangers of Relief

The statement has often been made that most symptoms are teleologic — that is, that they arise from useful intentions on the part of the body. When symptoms are useful or can be advantageously used to some purpose, it is clear that there are considerations against their relief. For example, the pain and muscle spasm that develop in the region of a fractured bone prevent tissue damage due to movement of the bones. Beyond this, it has been argued that the treatment of symptoms may itself introduce fresh sources of difficulty. This is true even for such a natural device as rest. Drugs may induce toxic or allergic reactions. Such complications of the treatment itself may be far more undesirable than the symptom.

Some fear that if physicians aim to relieve the symptom, they will lose the intense interest and the consequent precision in the art of diagnosis that are essential if they are to treat the cause of disease. This is not a real danger, because an understanding of the disease, its causative agents and its pathologic process are as essential to successful treatment of the symptom as to understanding of the mechanism of the symptom itself.

The possibility that relief of symptoms will interfere with or delay the precise diagnosis must also be considered in the management of an undiagnosed illness, especially if the development of the symptoms may have a bearing on the diagnosis. But if the pharmacologic actions of the drug used to treat the symptom are taken into account, this objection is usually academic. There are usually ways of observing the course of disease other than through the patient's distress; in pneumonia, for example, physical findings are far more revealing than the fever curve. And when the symptom is really useful, it is often possible to modify its intensity without suppressing it completely.

The Nurtured Symptom

There are many patients who, in one way or another, make social or psychic use of distress. These are patients who seek out symptoms and nurture them lovingly, engendering them because, for them, particular symptoms have special value. Patients may deliberately induce a symptom to distract attention from or to wipe out the appreciation of another and, to them, less acceptable symptom. Or they may positively embrace a symptom because it is more acceptable to them than normal function, or complain of symptoms to get attention or perhaps drugs. These are patients who, if relieved of one symptom, will promptly attach themselves to another or who, failing that, may react with some psychic difficulty. Many are resistive to therapy and may end as problems in overdosage. They are, clearly, patients to be distinguished at the outset of therapy.

Improvement of Function

Physiologic function may be directly disturbed by distress and corrected by its relief. As already mentioned, many reflex and adaptive reactions initiated by distress begin by being both protective and useful, but become so exuberant as to exceed usefulness. This is a boomerang that turns a protective mechanism into a pathologic process.

Mechanisms of Relief

Symptoms may be attacked on five different fronts, which are often closely allied or combined. Therapy of symptoms may be concerned with their specific mechanism of production; their perception; their reception or acceptability; and the response of the patient to placebos. A fifth method, suppression of the capacity of the organism to react to injury — a special attribute of cortisone and ACTH — has very special application, and will not be considered here.

Specific Relief

Specific relief of a symptom is a different matter from specific cure of a disease. The former attempts to abolish only the immediate mechanism of the symptom itself. Specific relief of a symptom may therefore be obtained without influencing the course of the disease itself. So far as the treatment attacks the mechanism of symptom production only, this form of therapy has no direct influence on mood, mental activity or attitude.

Pneumonia may be cured with penicillin, which will also relieve pain due to the pleurisy that may develop during the course of the disease; but this is specific treatment of the disease rather than of the symptom. Specific relief of a symptom is exemplified in the action of nitroglycerin to alleviate the angina of effort. This drug does not influence the ultimate cause of the symptom, arteriosclerosis, but it does affect the mechanism of the syndrome — namely, the spasm of the coronary arteries that causes the pain. This is a highly specific mechanism of pain relief and does not apply even to such closely related chest pains as those caused by myocardial occlusion. By and large this is the most desirable form of symptomatic therapy.

Symptom Perception

Symptoms may be obtunded or made less severe by depression of the patient's perception of them. Such depression may be highly specific and dull only the appreciation of the particular symptom, or it may

be so general as to involve the appreciation of all sensations — which, carried to its extreme, is represented by general anesthesia. Such relief is often selected because it is practical when an attack on the mechanism of symptom production may be dangerous, or because suitable drugs are not available or specific relief is too brief or too long delayed.

Most precise investigation of the effects of drugs on the threshold of symptom appreciation or perception has dealt with the pain experience. Perception of headache may be comfortably depressed with a dose of aspirin — despite the fact that the cause is untouched. In this instance the depression of perception is highly particularized. It is questionable, however, whether perception of symptoms other than pain can be dulled without, at the same time, dulling general perceptiveness, reflex reactivity and mental acuity to a degree that makes skilled work impossible and free activity hazardous. This, of course, poses an important practical problem. It seems, therefore, that although depression of perception may often seem desirable, its greatest use lies in relieving pain; for other symptoms, simultaneous effects on other sensations, on reflex actions, on mental acuity and on mood and affect challenge its efficiency.

Symptom Acceptance

Relief of symptoms may be provided by a rise in the level of what may be called the threshold of symptom acceptability. It is an assault on the psychic reaction to symptoms designed to make particular forms of distress or unusual sensation more tolerable. Such an approach is therefore directed toward the patient's mood — his attitude to the symptom — rather than toward the symptom itself, its mechanism or its perception. The most exaggerated example of this kind of relief is prefrontal lobotomy for intractable pain. In such cases the patients are still aware of the pain, but the once intolerable sensation has become acceptable.

It is well to remember that relief of symptoms by altering mood has inherent dangers greater than the other types of relief just discussed. They are more likely to induce dependence or habituation. Relief of this type is safe only when the extent of the psychic component of the patient's distress and his reactions to it have been determined. The justification for treating a symptom by making it more acceptable depends on such features as the medical usefulness and dangers of the symptom, the dosage of drugs used, the hazards in using the particular drug long enough to make the symptom acceptable, the requirements of the patient to be alert and the dangers of addiction and habituation inherent in the drug and in the personality of the particular patient.

"Placebo" Relief

So far as the very fact of treatment carries the symbolic significance of medicine and the reassurance that something positive is being done, all treatment provides a potent psychic element in relief — all treatment has, at the very least, the psychic effects that may follow a placebo. This influences the perception as well as the acceptance of the symptom. It is affected by the rapport between the patient and the physician and by the meaning to the patient of the drug itself, as well as by additional forces that are brought into play.

Combinations

A combination of devices for the relief of symptoms is implicit in all measures of symptom relief, other than that of placebo. There is no way of sloughing off the favorable psychic effects of attention and reassurance and the placebo effects of active and potent drugs. Many drugs such as morphine and codeine have inseparable pharmacologic effects on both perception and tolerance of distress. It is the mixed action of drugs in relieving symptoms that makes it such a difficult matter to evaluate drug effects and to determine the nature of their action when they are used for this purpose.

Prevention

It is generally assumed that it is easier to prevent symptoms than to treat them after they have appeared or that it requires less drug. In practice there are times when the opposite is true. Prophylaxis and relief of established symptoms are really different therapeutic problems rather than degrees of the same problem. The treatment and prophylaxis of symptoms differ in aim, in the operation of psychic forces and in the meaning of dosage response. In addition, prophylaxis may involve special dangers, cumulation, tolerance, habituation, dependence and addiction.

Degrees of Relief

The goal to set for the relief of the symptom is determined not only by the symptom but also by the drugs available. If the symptom serves a useful medical purpose and is negligible in terms of anxiety, discomfort or disturbing adaptive reaction, the need for relief is small; correspondingly, the degree of relief to be contemplated is also small. If, on the other hand, the symptom upsets normal function or induces disturbing adaptive reactions, relief, at least sufficient to control these responses, should be considered. Between the extremes of no relief and complete relief of all distress lie combinations of discomforts and attendant dangers. The extent to which various methods of achieving relief may be safely used sets the limits to their use.

In situations in which the specific attack on the symptom may involve hazardous changes in function, the modification of the patient's attitude may be useful even though the symptom itself is not obtunded.

For example, one cannot contemplate suppressing the cough reflex in a case of bronchiectasis because of the danger of accumulated sputum; however, if the patient is adequately sedated he may continue to cough, but find it so much less disturbing that it is tolerable. It is unfortunate that physicians do not more commonly use the same approach in the treatment of such severe pain as that of acute myocardial infarction, which is among the most difficult to relieve completely. The large doses of morphine that would be necessary to obtain full relief might also depress respiration. However, morphine given in relatively small dosage to alter the patient's tolerance to the pain may remove from the pain much of its shocking quality as well as its capacity to induce anxiety and restlessness; from this point of view, the lesser but safe action of the smaller dose of morphine may induce the most satisfactory therapeutic effect possible under the circumstances.

Conclusions

In treating the symptom, one deals with a living process of which the basic disease is only one aspect. Far from being elementary, the symptom is a complicated expression with fuzzy borders, and it provides no easily perceived objective criteria for the evaluation of treatment. The art of this kind of evaluation is elusive, for not semantics but a highly involved human process separates the physiologic disturbance from the communication the patient makes to his physician.

The drugs now available are the most effective yet discovered for making the patient more comfortable. To use any of these drugs without interfering with the course of therapy of the basic disease, one must know the pharmacologic properties of the particular drug, the physiologic functions that it depresses or stimulates, the functional disturbances that it can ameliorate and the untoward effects that it can have. One must not only know the physiologic basis of the symptom, but also — and of equal importance — weigh and estimate the complex of forces it can set in motion. Only with understanding of the many features of drugs, coupled with awareness of and feeling for symptoms, can one determine when a drug is indicated and when it is contraindicated in the cases with identical symptoms. Only with such a background is it possible to know when a patient with a given symptom is more likely to respond well to one drug and be resistant to another, when it is advisable to interrupt the mechanism that causes the symptom, when it is better to treat the patient's attitude toward it and when it is more practical to treat his ability to endure a symptom than to treat his threshold of appreciation of it.

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MEDICAL PROGRESS

GASTROENTEROLOGY (Concluded)*

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BOSTON

Colon

The diagnosis of colonic disease still depends on clinical findings, proctosigmoidoscopy and x-ray examination chiefly with the barium enema. A more general use of proctosigmoidoscopy has been adopted particularly as part of a complete medical survey and in all gastrointestinal cases in which rectal symptoms or bleeding is reported.

Several improvements in the x-ray examination of the colon have been described during the past five years. The development of newer methods has been stimulated chiefly by an effort to improve the detection of small intraluminal tumors. Two methods in use for several years are the employment of a dilute contrast medium and the addition of tannic acid to the barium enema for a more complete expulsion and improved postevacuation film for visualization of the mucosal pattern.

The double-contrast enema is still an efficient method of examination, and refinements in this technic have been developed by several workers in this field. Varying positions to shift the air and barium suspension from one loop to another have been found to yield satisfactory results although the method requires so much time and so many exposures that it obviously cannot be used as a routine examination. Stevenson and Wilson[41] have set up some practical indications for the use of the double-contrast technic.

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Visualization of the sigmoid, where a preponderance of new growths occur and where examination is most difficult because of overlapping loops, has been found by Moreton[42] to be facilitated by the Chassard–Lapine or "sitting position."

The importance of colonic dysfunction in practical clinical medicine has become more generally recognized than ever before. In this field the psychosomatic phase of gastroenterology is conceded and as far as possible therapeutically managed, but the somatic and even somatopsychic phases of this condition are likewise recognized and treated. The former gastrointestinal invalid is no longer regarded as inevitably a hopeless neurotic.

As far as organic disease in the colon is concerned, polyps continue to be the subject of active interest on the part of clinicians treating colonic disease. Although Rider et al.[43] point out that there is still no conclusive direct evidence that benign adenomatous polyps undergo transition to cancer, the weight of circumstantial evidence for an association between carcinoma and polyps is so great that polyps are generally regarded as potentially premalignant lesions.

For polyposis of the colon the procedure of subtotal colectomy with ileosigmoidostomy and periodic fulguration of any polyp that recurs in the retained rectum and sigmoid has been evaluated by Everson and Allen,[44] and their conclusion is that preservation of the rectum and sphincter rather than total colectomy is worth the additional risk of malignant degeneration.

Multiple incisions in the colon, with inspection in both directions through an endoscope, were reported to be of value by Deddish and Fairweather,[45] who found lesions other than those shown by roentgenogram in 50 per cent of cases. In their series of 99 cases there were no deaths but some increase in morbidity consisting of postoperative ileus, abdominal abscess, wound infection and hemorrhages.

Ulcerative colitis, with its etiology still obscure, remains a baffling and complicated clinical problem, but some progress has been made in its management. In the medical treatment the use of the steroid hormones has been the most outstanding development, and there are several clinical studies based on fairly large groups of patients, all indicating that no other therapy has produced such markedly favorable effects as rapidly and as uniformly.[46,47] Some important undesirable effects, however, such as giant ulcerations of the mucosa[48] and perforation have been reported. There is also considerable evidence that secondary bacterial invasion with necrosis may be promoted by steroid therapy even during symptomatic improvement. Although clear-cut indications and contraindications for the use of steroids have not yet been established, Bargen[49] concludes that many patients with colitis should not be given this form of treatment.

Some new concepts of the surgical treatment of the severe, complicated, septic or fulminating case have led to the employment of combined ileostomy and total colectomy, which removes the primary pathologic process, replacing ileostomy alone, which fails to do so. Successful applications of this more radical but logical approach to a serious problem have been reported. For chronic cases in which surgery is indicated Scarborough[50] recommends a single-stage operation of complete proctocolectomy and ileostomy.

Improved technic in the construction of the ileal stoma and in the use of newer ileostomy appliances has contributed to the successful management of this operative condition and thereby to the happiness of the patient with a permanent ileostomy.

A relatively rare postoperative complication called *pseudomembranous enterocolitis* has aroused considerable interest particularly since antibiotic therapy has been suspected as an etiologic factor. Statistics reported by Pettet et al.[51] from the Mayo Clinic, however, fail to indicate any increased incidence since the beginning of the antibiotic era, although bacteriologic studies have frequently shown an overgrowth of staphylococcus or proteus, which are thought by some to produce an enterotoxin that in turn produces a choleralike syndrome, usually fatal. Some evidence has been reported that staphylococcal overgrowth and toxemia is the etiologic factor. Lowbeer,[52] however, in a review of the known facts concerning the disease, concludes that the basic disorder is a breakdown of tissue relative to severe stress and shock and poor adrenal response and that the mucosal necrosis is increased by pathogenic staphylococci, which grow rampant on the necrotic tissue, particularly when other organisms have been eliminated by antibiotic therapy. Prohaska et al.[53] have reported remarkable success in the treatment of a small group of patients with ACTH, results that they interpreted as evidence against the bacterial origin of the disease. The discussion of this condition is important in that in any case of severe postoperative diarrhea this diagnosis should be considered and if fever, toxicity and signs of circulatory collapse develop, treatment should be prompt and energetic and should include ACTH, antibiotics based on cultures and sensitivity tests, fluid and electrolyte corrections and antishock and other supportive measures.

Preoperative cleansing and sterilization of the colon in preparation for surgery has recently become standard practice. In his outstanding studies, Poth[54] has laid down the essential properties of an acceptable preoperative antiseptic. He has found a combination of neomycin and Sulfathalidine given according to a carefully prescribed program to be the best. He also reports for infected cases the use of 200 to 300 ml. of 1 per cent neomycin solution during operation both in the abdominal cavity and injected into the lumen of the bowel. He advises that neo-

mycin be restricted to this particular use to avoid the production of resistant strains of organisms.

In chronic and recurrent diverticulitis of the colon the trend has been toward more frequent employment of surgical resection. Papers by Barborka and Texter[55] and by Ransom[56] describe the most recently accepted surgical approach to this disease. Resection with primary anastomosis is the operation chosen for uncomplicated diverticulitis, cases with fibrostenotic lesions and those in which carcinoma cannot be excluded.

The differential diagnosis between diverticulitis and carcinoma on roentgenologic and clinical data is still regarded as reliable in a majority of cases but in some cases inconclusive. Colcock and Sass[57] have pointed out the difficulty of differentiation at the operating table, and in their opinion, after adequate but inconclusive preoperative study and if the surgeon also cannot exclude cancer, a wide resection is indicated.

The somewhat controversial point of whether diverticulitis without cancer can cause gross bleeding seems to be settled in the affirmative. The subject has been well documented by Hoar and Bernhard,[58] who report 4 cases of diverticulitis with exsanguinating hemorrhage.

Congenital megacolon, or true Hirschsprung's disease, has acquired new surgical interest through the modern concepts of its etiology and pathology discussed in detail by Keefer and Mokrohisky,[59] who describe methods of demonstrating the aganglionic segments that cause the characteristic chronic obstruction. They report that 90 per cent of cases have short zones of aganglia and 10 per cent have long segments extending from the rectum to the splenic or hepatic flexures, with 1 of their cases showing two separate aganglionic areas.

Swenson et al.[60] describe the technic of biopsying the muscular coats of the rectum for the diagnosis of megacolon and cite its special value in the newborn infant and in cases in which other diagnostic criteria are inconclusive.

In the field of cancer of the colon and rectum recent interest has been focused on the mechanism and routes of spread of malignant cells and upon operative procedures designed to diminish postoperative recurrences. The most important contributions on these subjects have only recently been cited by Welch.[61]

Pancreas

The diagnosis and treatment of pancreatic disease are still impeded by a lack of accurate and clinically feasible tests of function, in spite of availability of secretin, technic of collecting pancreatic secretion from the duodenum via double-lumen tubes and measurement of pancreatic enzymes in the blood.[62] Furthermore, it is also as yet impossible to outline the pancreatic ductal system or its blood supply by radiography.[63,64]

A better understanding of pancreatic disease, however, has resulted in the last decade from the original work of Comfort et al.[65] in 1946, which has been confirmed by numerous subsequent reports. The designation chronic relapsing pancreatitis was given by them to the disease characterized by repeated sublethal episodes of acute pancreatitis not necessarily associated with biliary-tract disease, and its pathology was described as ranging in severity from pancreatic edema to necrosis. The accepted theory of etiology is that some degree of obstruction occurs to the flow of pancreatic juice, whether by psychophysiologic spasm of the sphincter of Oddi[66] or by involvement of one or both of the major intrapancreatic ducts.[67] The exact trigger-mechanism role of reflux of bile into the pancreas or hyperstimulation of secretion secondary to alcohol ingestion or meals difficult to digest remains hypothetical.

Except for the endocrine disorder, diabetes mellitus, and such rare entities as hyperfunctioning adenoma, annular pancreas, fibrocystic disease and noninflammatory cysts, the bulk of pancreatic disease is now recognized as either inflammatory or malignant.

Aaron and Milch[68] have described in excellent detail the symptoms characteristic of *acute pancreatitis,* pain in retrosternal or interscapular areas or in the left side of the chest or left flank characteristically unrelieved by vomiting occurring in 80 per cent of cases and the development of shock, cyanosis, distention and cutaneous signs. Pollard and Bolt[69] mention some of the newer tests used in diagnosis. It is generally recognized that in the diagnosis of acute pancreatitis, other diseases of the upper abdomen must first be excluded.

A plain film may demonstrate local ileus in duodenum or ileum, calcifications in pancreas, biliary tract or kidney and fluid above or fluid or air below the diaphragm. Serum amylase of eight to ten times the normal range, elevated blood sugar, antithrombin titer and serum lipase level and the finding of pancreatic enzymes or sugar in the urine are additional evidence of involvement of the pancreas. Intravenous cholangiography may help differentiate the pain of pancreatitis from that due to intermittent bile-duct obstruction.

Medical treatment, begun as soon as the diagnosis is suspected, is preferred to surgical intervention. Rest, relief of pain, maintenance of blood volume, correction of blood chemical abnormalities and guarding against complications are the best therapeutic measures. Relief of pain alone may reduce vasoconstriction and prevent pancreatic edema from becoming necrosis. Cattell and Warren[70] suggest continuous or intermittent epidural procaine anesthesia if Demerol or morphine is ineffective. Rest to the pancreas is attained by prevention of gastric se-

cretion from entering the duodenum through a nasogastric tube and suction, thus preventing or alleviating duodenal and jejunal ileus. The intravenous use of a carbonic anhydrase inhibitor (Diamox) or anticholinergic drugs administered intramuscularly may decrease the volume of pancreatic secretion.[71] Relaxation of the sphincter of Oddi is most effectively attained by papaverine, nitroglycerin, amylnitrate pearls or atropine. Complete recovery from the initial attacks may be expected because of the tremendous reserve capacity of the pancreas.

Additional means toward prevention of complications consist in inhibiting bacterial growth in the reactive fluid secondary to localized peritonitis and include the use of antibiotics, the current favorites being penicillin and streptomycin. For abscess formation, hematoma, spreading peritonitis or cysts, surgical intervention is indicated.

Many writers, including McDonough[72] and Collins and Owens[73] have described the episodes of variable intensity recurring in the same patient that constitute chronic relapsing or recurrent pancreatitis. Pain is the most important symptom, and it varies in intensity from a nuisance distress to complete disability with narcotic addiction.

Mild attacks may require only sedation, anticholinergics and analgesics, and during remission decision may be made whether medical or surgical treatment is indicated. Medical management as described by McDonough[72] is in brief as follows: omission of alcohol, a nonirritating diet modified in carbohydrate content if diabetes is present, avoidance of gastrointestinal irritants and use of antispasmodic drugs, bowel hygiene, control of diabetes, and use of pancreatin to prevent fecal loss of fat and protein.

Surgical treatment was recently described by Collins and Owens,[73] who quoted from Crile a choice of ten operations with direct and indirect effect upon the pancreas which could be used for chronic relapsing pancreatitis, commenting that when many different forms of therapy are advocated, it is because none of them is satisfactory in all cases. Cattell and Warren[70] recommend one or a combination of the following four operations directly involving the pancreas: transurethral sphincterotomy and exploration of the duct of Wirsung and the duct of Santorini; distal pancreatectomy; anastomosis of the duct of Wirsung to the stomach or jejunum; and pancreaticoduodenal resection. They choose the one or the combination of these operations that is best adapted to the individual case.

Cancer

Progress in the diagnosis of pancreatic cancer has paralleled that made in the detection of chronic pancreatitis. Cancers arising in the head of the pancreas, ampulla of Vater and distal common duct present similar problems and should, therefore, be considered together.

In diagnosis of cancer it is now generally recognized that the concept that malignant lesions of the pancreas and the periampullary area are characterized by painless jaundice is erroneous. In fact characteristic pain is the most frequent presenting symptom. If jaundice precedes pain, particularly in the absence of fatigue, weight loss and digestive disturbance, in a patient in the cancer age group, this patient should be promptly explored with a diagnosis of carcinoma of the periampullary area with the expectation of cure by pancreaticoduodenal resection.

When carcinoma of the pancreas is suspected on the basis of presenting symptoms the same tests and roentgenographic aids employed to detect chronic inflammatory disease should be used. Wise and Johnston[74] recently pointed out that careful attention to minor details of radiographic interpretation can lead to early diagnosis of cancer. They stress the fact that the internal aspect of the duodenal loop outlined in various views by barium and air, and with consideration of the effects of visceral pressure and gravity, may suggest a pancreatic lesion before the loop is characteristically widened and when the lesion may still be resectable.

Surgical extirpation remains the only curative therapy. The five-year survival rate of patients in whom pancreaticoduodenal resection was technically possible for carcinoma of the head of the pancreas is only 5 per cent; that for carcinoma of the ampulla of Vater is 30 per cent.[70]

Liver

Most of the recent articles on liver disease have been a recapitulation of previously published work or an attempt to clarify it. In conjunction with the present report on progress in gastrointestinal disease two recent papers may be mentioned. In 1955 McDermott, Wareham and Riddell[75] discussed the history of studies on hepatic coma and of the events leading up to their own studies. The authors divided cases of hepatic coma into acute spontaneous, acute exogenous and chronic cases. It has been their experience that in the acute spontaneous cases, described as "patients with advanced liver disease who had central-nervous-system symptoms without any precipitating factors," no method of treatment has been satisfactory or has been able to prevent death as a result of hepatic coma. In the acute exogenous group, there are precipitating factors such as the administration of ammonium chloride, acute gastrointestinal hemorrhage or a high-nitrogen diet, any of which will precipitate the onset of coma in cases with advanced liver disease. The authors determined the level of the blood ammonia,[76,77] the normal value being in the range from 40 to 80 microgm. per 100 ml., and for treatment the administration of L-glutamic acid or the sodium salt of L-glutamic acid, sodium glutamate, intravenously. The dose either by mouth or intravenously is approximately 25 gm. daily.

The L-glutamic acid has the property of reducing the blood ammonia level toward more normal values, and in cases in which this is efficient, the patient can be returned to consciousness and makes a rapid recovery. The authors suggest a differentiation of "spontaneous hepatic coma" from "exogenous hepatic coma," the latter referring primarily to the syndrome of ammonia intoxication.

Foulk et al.[78] have contributed another interesting study on hepatic coma and have reviewed the records of 52 patients with this condition. Coma was most frequent in those with primary parenchymal hepatic disease, but it also occurred in patients with obstructive jaundice and with neoplastic disease of the liver. The onset of coma in their group appeared to be either insidious or quite rapid. They describe a "flapping" of the fingers as part of the tremor at the onset of the disease. Treatment was symptomatic, with parenteral feeding and maintenance of fluids and the electrolyte balance.

Conclusions

Progress in gastroenterology, as indicated by this report, has been promoted in this mid-twentieth century by several advances in the field of general medicine. The etiology of certain serious gastrointestinal diseases such as peptic ulcer, regional enteritis and ulcerative colitis is still obscure, but investigative work and clinical observations accumulate and hopefully will enlighten this area of darkness. The use of isotopes in tracer doses for diagnosis is still in its infancy — but in an infancy that suggests the promise of growth and the possibility of this development for therapy. Accuracy of diagnosis of all gastrointestinal disease has kept pace not only with progress in clinical observations but also with the technical advances of radiology, a substantial and dependable aid to gastroenterology for half a century. The more recent diagnostic procedures, endoscopy and cytologic studies, have added in considerable measure to the success of diagnosis. Therapy has been advanced by extensive pharmaceutical research and developments based on gastrointestinal physiology. Inspired and sound investigative work in all phases of gastroenterology and continued clinical observations accurately reported give promise of a bright future in this broad and fertile field.

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MEDICAL INTELLIGENCE

THE ROCKING BED AND HEAD POSITION*

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UNTIL November, 1955, we had been using the rocking bed in the conventional manner as an aid in breathing for the patient with chronic poliomyelitis who was dependent upon a respirator. We had assumed that for maximal effect the head must come below the horizontal position when rocking. During this month, a patient (W.B.) returned for a periodic outpatient checkup and reported that she no longer could "rock" with her head flat. The reason she gave was that she just could not get enough exchange of air in that position and, consequently, was short of breath while attempting to rock.

In an effort to help her continue to use the rocking bed as an aid, we elevated her head to 15° on the oscillating bed and recorded her tidal air at that position. Remarkably enough, it was greater than with her head in the supine position. The difference enabled her to use the rocking bed successfully. Shortly after this patient's visit we observed the same phenomenon in another patient (E. L.), who could not rock with his head flat. His measurements showed that he did much better with his head elevated to 30° on the oscillating bed.

These 2 patients stimulated us to do random checks on the rocking-bed ventilation patterns of 9 other respirator patients with chronic poliomyelitis.

CLINICAL SUBJECTS

The group of patients tested all had severe poliomyelitis as far as motor and respiratory functions were concerned. Their vital capacities in the supine position ranged from 150 to 1600 ml., or 3 to 30 per cent of the predicted normal value. There was no increase in the vital capacities of these patients when they were sitting. All were patients at the University of Michigan Poliomyelitis Respirator Center.

METHODS

The ventilation patterns were recorded while the patients were using an Emerson rocking bed set in the third hole on the rocking arm. At this setting the head portion of the bed passes through an arc of 37°. With the bed in the supine position, the patient's head moved in an arc limited at 10° below and 27° above the horizontal plane. With the entire upper part of the bed set at 15°, the limits became 5° and 42° above the horizontal plane. At 30° the limits were 20° and 57° above the horizontal plane. While rocking the patient's head rested on a 4-cm.-thick pillow. The position of the legs was always flat (this position was chosen so that another variable would not be introduced). It can be said, however, that several patients were measured with both head and knees elevated and that the results were similar and, in some cases, better than those with the knees flat. Figure 1 shows the three positions used.

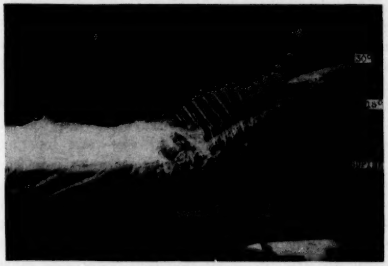

FIGURE 1. *Patient in Three Positions on the Rocking Bed.*

The rates of oscillation varied between 18 and 20 times per minute. Each patient was observed carefully for muscle assistance to breathing during rocking, and none could be observed.

In the study of this group of patients, a Sanborn closed-circuit BMR Spirometer with mouthpiece and nose clip was used to make the necessary recordings. They were taken on the ward, where the average temperature was 25°C.

RESULTS

Of the 11 patients who were measured by us, 8 had tidal air exchanges, with the upper part of the bed elevated to 15°, that were superior to those obtained when their heads were supine. One patient remained the same, and 2 patients had lower tidal air exchanges in this position.

Elevation of the upper part of the bed to 30° caused 7 patients to have greater tidal air exchanges; 1 remained the same, and 3 showed decreases from values recorded in the supine position. Table 1 summarizes these data.

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Discussion

Our results certainly are not what one would expect, since the principle of the rocking bed is dependent on movement of the abdominal viscera, with subsequent movement of the diaphragm.[1] The head-up position, seemingly, would limit this movement. Plum and Whedon,[2] in their evaluation of the oscillating bed, point out that when the knees are raised more than 10 to 13 cm. and the head more than 5 to 8 cm., diaphragmatic restriction occurs. A head elevation of 15° is 18 cm. above the horizontal, as measured from the end of the bed.

TABLE 1. *Results with Rocking Bed* Set at Three Positions.*

Patient	Vital Capacity in Supine Position	Tidal Air Exchange on Rocking Bed		
		in supine position	at 15°	at 30°
	ml.	*ml.*	*ml.*	*ml.*
K.M.	303	370	450	450
E.L.	300	242	420	450
W.B.	242	260	310	310
P.L.	515	400	465	420
D.Z.	515	570	660	600
A.K.	1600	480	525	450
W.H.	364	450	480	540
B.M.	333	400	450	450
N.S.	485	480	480	480
B.P.	150	420	400	370
S.E.	545	435	400	400

*Emerson rocking bed, set in 3d hole of rocking arm, with arc of rock 37°.

We are hard put to explain this increase in the tidal air volume, but offer one or more of the following suggestions as possible factors: the compliance of the lungs, diaphragm and rib cage certainly influences air exchange, and it is well known that patients with noncompliant chests find it difficult to breathe with any aid[3] (all our patients had good compliance curves, including the ones in whom no increase in the tidal air volume was encountered); compliance is increased by lessening of blood volume in the chest, — sitting accomplishes this to some degree, — and such changes may have been influential in our findings.

A difficult factor to measure is degree of relaxation or accommodation to the rocking bed. We have seen patients do poorly as far as ventilation is concerned when on a bed that is unsteady or one that vibrates considerably. Changing these patients to more suitable beds and rocking through identical arcs in the same bodily positions, we find that they often have an adequate air exchange in the new situation. We believe rocking with the head raised is conducive to more relaxation and perhaps helps increase air exchange.

Conclusions

Before the rocking bed is abandoned as an aid to breathing in some patients because of insufficient ventilation, one should try elevating the upper part of the bed to 15° or to 30° and measuring the patient's ventilation in this position.

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INCIDENCE OF PATHOGENIC SEROLOGIC TYPES OF *ESCHERICHIA COLI* AMONG NEONATAL PATIENTS IN THE NEW ENGLAND AREA*

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ANTIGENICALLY homogenous strains of *Escherichia coli* (var. *neopolitana*) were isolated from infants with summer diarrhea in London by Bray[1] in 1945. Since then several of the four serotypes of *Esch. coli* have been found in hospital outbreaks of infantile gastroenteritis throughout the world,[2-10] and the pathogenic role of some of these serotypes has been further demonstrated by administration of live cultures to adult volunteers.[11-13] In epidemics the newborn infant is extremely susceptible whereas older infants are relatively resistant. Although outbreaks have been characterized by a high infectivity rate among infant contacts, there have been differing reports on the frequency of sporadic clinical infections. In Ontario Hinton et al.[14] examined stools from 47 patients in sporadic cases of infantile gastroenteritis and found that 24 had positive cultures for *Esch. coli* (serogroup 0111). In Pittsburgh, however, Stock and Shuman[15] noted that sporadic diarrhea due to pathogenic *Esch. coli* serotypes was uncommon, and this has also been the experience in both the Boston Lying-in Hospital and the Children's Medical Center in Boston.[16]

The association of pathogenic serologic types of *Esch. coli* with asymptomatic infections and carrier states has shown marked variation in different areas. In Denmark Dupont[17] examined fecal samples taken from 940 healthy infants under one year of age, and

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all were negative for two pathogenic serotypes of *Esch. coli*. He also examined routine rectal swabs obtained from 538 neonatal infants before discharge from a lying-in hospital, with similar negative results. Graber and Dunlop[18] investigated hospital pediatric and nursery patients in Denver and found no established pathogens or suspect colitypes among 410 non-diarrheal cases, and Taylor et al.,[5] in England, found none among 208 controls. On the other hand, in Aberdeen, Giles et al.[19] examined stools from 271 non-diarrheal infants and found that 7 were excreting pathogenic serotypes of *Esch. coli*. In Glasgow Shanks[20] found 4 asymptomatic infections among 101 children in the first year of life. In Oxford Payne and Cook[21] found *Esch. coli* (serogroup 0111) in 17 children, 11 of whom had no diarrhea, and in London Cathie and MacFarlane[22] reported that infection with this serotype was as common in controls as in infants with diarrhea.

In view of the variation in incidence of asymptomatic infections with pathogenic serotypes of *Esch. coli* reported from different areas, and because there have been few reports on the incidence of asymptomatic infections during the neonatal period, it was decided to carry out routine stool cultures on all admissions to the nursery for newborn full-term and premature infants at the Children's Medical Center in Boston.

Method

The newborn nursery has accommodations for 14 infants. Each infant is enclosed in an "isolette," which is provided with an air feed drawing from the outside air under positive pressure. A strict barrier nursing routine is enforced, and all formulas are terminally sterilized. All admissions are from other hospitals, and patients with a history of vomiting and diarrhea are excluded from this unit. As soon as practicable after admission, and never later than the third day, a stool sample was collected in a sterile glycerine preservative medium and sent without delay to the laboratory. Bacterial examination was carried out by Dr. Robert A. MacCready at the Diagnostic Laboratory of the Massachusetts Department of Public Health up to December 1, 1955, and thereafter at the Routine Clinical Laboratory at the Children's Medical Center. Each specimen was examined for salmonella, shigella, and four pathogenic serotypes of *Esch. coli* (0111:B_4, 0127:B_8, 026:B_6 and 055:B_5), using the method described by Edwards and Ewing.[23]

Results

Between July 1, 1955, and January 1, 1956, the stools of 121 infants were examined. Of these infants 114 were under one month, and 91 were under one week of age. The group consisted of 64 males and 57 females who came from hospitals in 23 centers of population in Massachusetts, Maine and Connecticut. The average duration of stay in the nursery was eleven and four-tenths days.

All stools were negative for pathogens with the exception of those obtained from 2 male infants, both under the age of one week. The first positive result was obtained from an infant born on July 8, 1955, who was admitted to the nursery on the day of birth from an outlying hospital because of a positive Coombs test. A stool specimen was obtained on July 11 and was reported positive for *Esch. coli* (026:B_6) two days later. The infant was then transferred to an isolation cubicle and given neomycin as a precautionary measure. During his stay in the hospital he thrived well, took his feedings ravenously, did not vomit and had no diarrhea. Nose and throat swabs were negative, and after treatment with neomycin, the stools were also reported as negative.

The second positive result was obtained from an infant born on September 19, 1955, in another outlying hospital and transferred to the nursery on September 22 because he was reluctant to take feedings owing to a brain injury at birth. A stool specimen was taken on the day of admission and reported as positive for *Esch. coli* (055:B_5) on September 24, when he was isolated and given neomycin. During his stay he did not vomit, and he never passed more than four stools a day, which were of normal color, consistence and odor. Weight gain was slow because of reluctance to suck, but eventually he was discharged thriving satisfactorily.

Discussion

The finding that two out of a group of 91 infants under one week old were excreting pathogenic *Esch. coli* when admitted to a neonatal unit where every effort is made to exclude infants having a history suggesting gastrointestinal infections, emphasizes the vigilance that must be maintained in such units. It also seems that the routine examination of neonatal admissions for pathogenic *Esch. coli* is a justifiable measure. In the present state of knowledge it can be assumed that either of the infected infants in the group examined could have given rise to an explosive outbreak of gastroenteritis carrying a high mortality.

It is of interest that neither of the infants with positive cultures had diarrhea, vomiting or pyrexia. Undue importance should not be attached to this finding, however, for both were given neomycin in a dose of 50 mg. per kilogram of body weight per day for six days when a positive report was received, and this may have aborted the infection, Stultberg et al.[24] having shown that the excretion of pathogenic *Esch. coli* may precede by some days the onset of clinical signs.

Unfortunately, maternal stools were not examined; such a procedure might have thrown some light on the origin of the infection that was detected in both infants during the first days of life. It would also

have been of interest to have determined the relevant titers against *Esch. coli* in both mothers and infants, since this might have provided an additional reason for the absence of clinical signs.

Summary

The incidence of asymptomatic infections with pathogenic serologic types of *Escherichia coli* reported from different areas is reviewed.

Stools were collected from 121 infants on admission for causes other than diarrhea and examined for four pathogenic serotypes of *Esch. coli*. The group consisted of 91 infants under one week and 30 infants between one and six weeks of age. Two male infants, both under one week old, were found to be excreting *Esch. coli* (serotypes 055:B_5 and 026:B_6 respectively). No pathogenic serotypes were isolated from infants over one week of age.

In view of the occurrence of apparently asymptomatic infections with pathogenic *Esch. coli* it is suggested that routine examination for these pathogens among infants admitted to neonatal units is a desirable preventive measure.

We are indebted to Dr. Harry Shwachman, of the Children's Medical Center, and Dr. Robert A. MacCready, of the Massachusetts Department of Public Health, for the bacteriologic and serologic examinations and for much helpful advice.

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DOCTORS AFIELD

Walter Henry Chapin

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WALTER Henry Chapin was a very learned physician. His inquisitive mind and his burning thirst for knowledge drove him into many fields. He was no dilettante. Into whatever realm of learning he ventured — and they were many — he delved deeply until he outdid many a man whose special field he invaded.

Born in Springfield, Massachusetts, on March 6, 1859, Dr. Chapin added renown to a family name illustrious in the annals of that city. He received from Yale College the degree of A.B. in 1880, and from the College of Physicians and Surgeons (Columbia) the degree of M.D. in 1883. After an internship in Bellevue Hospital, New York, he practiced in Springfield until his death on April 2, 1939.

Dr. Walter Chapin's forte was diagnosis. As always it was the puzzle that fascinated him. In solving it he relied chiefly on his own eyes, ears and fingers. His keen, analytic mind marshaled his observations into their relative order of significance and importance until he had a solution he could uphold against all attacks. If later he was proved wrong — which was not often — he was severely critical of himself, not so much because the patient suffered unduly, or even died, but because his observations or his analyses or both were erroneous, and he never rested until he had exposed their fallacies. Once he had made a diagnosis, however, his interest in a patient was apt to wane. If treatment had posed him another puzzle, he would have won even greater renown. Therapy of his day was for him too empirical — too unscientific. He was pretty much a therapeutic nihilist. If the half dozen or so drugs in which he had faith proved unavailing, the patient would die anyway, so why, he wondered, do more than keep him comfortable until the inevitable end?

Dr. Chapin's pursuit of knowledge took him far beyond the bounds of his profession. Language was a lifelong challenge. Ever at his elbow were an unabridged English dictionary and Latin and Greek lexicons. He not only read these two ancient languages easily but also combed them for the roots from which English derivatives spring. It was these intensive studies, perhaps more even than wide reading of classical literature, that awarded him an outstanding command of English. He did not often speak, but when he did his grammar was faultless, his choice of words exact, and his sentences crisp, concise and forceful. He seldom wrote, but the prose he left is in the lean, brisk style that says most in the fewest words. He was also no mean poet. Unfortunately, most of his poesy was only for the private medical club to which he belonged and, though sparkling and in true poetic form, is unseemly for publication. That his poems were not always so handicapped, however, is evidenced by this gem:

Witch-hazel

November's chill and leaden days are here;
The fallen leaves and withered grass proclaim
That winter comes. And yet the yellow flame
Of brave witch-hazel lights the passing year.
Courageous friend, Though bitter storms are near,
Though distant spring seems but an empty name
Your subtle perfume and your petals shame
Me for my blindness. You with vision clear,
Beyond the dark and frigid winter see;
And set your fruit prepared against the days
When it shall ripen in the summer sun.
I pray my faith, inspired by you, may be
So keen of eye that through this doubtful haze
I see my life renewed when this life's done.

Close beside his dictionary and lexicons were a Bible, a Greek New Testament and a bulky concordance. That he might himself have access to original sources, he mastered Hebrew. He studied the Bible not so much as a religious experience as a profound literary inheritance. He ranked high as a Biblical scholar and critic, seeking answers to the book's origins, issues and contradictions. He was no carping iconoclast, no cynical unbeliever, no churchgoing hypocrite. He believed in God but not in the kind of God many did — a belief more ethical perhaps than religious, but rational withal and befitting its professor.

While adding a reading familiarity with French and German to his linguistic attainment, he explored many a scientific field. Mathematics, astronomy, geology and biology were never-ending challenges to his quest for knowledge. Not at all infrequently he reduced the answers for tricky puzzles and riddles to algebraic equations or geometric symbols. He called the stars by name and knew where and when best to see them. He knew the birds, the insects and the beasts of forest and field, their habits and habitats. He called the flowers of meadow, swamp and mountainside by name and knew their structures and where to find their hiding places. The rocks and clay banks were for him open books of millions of years of history. None of all this was mere book learning. It came from firsthand observation on many a far-flung tramp through verdant valley, over rocky hillside and into deep-cut gorges, from all of which he carried home scores of specimens for analysis and microscopical study. His mind was a well stocked warehouse of learning. It was no idle, dusty storage loft, but a living treasure vault whose ordering was his own delight and lasting satisfaction. He was no crusty pedant nor blustering showman. The pity of it is that so much learning went with him. He was not a teacher. He was too impatient with slow thinking, too intolerant — sometimes rudely so — of ignorance. Only with a few, and not often with them, did he with kindly interest share his vast fund of knowledge. If the urge to teach had been added to his virtues, many a man who knew him would be thereby the richer.

For relaxation he seized eagerly upon whatsoever afforded a problem. Jigsaw puzzles he turned upside down. The pieces were too easily assembled if aided by the picture they portrayed. For crossword puzzles he disdained to use the diagrams: they made the solutions too easy. Fascinated by the beauty and texture of Oriental rugs, he learned the intricate knots used in their making and himself wove a small one. The puzzle that interested him most, however, baffled him: the origin of life. He pondered long and deeply each and every theory advanced to resolve that mysterious phenomenon, picked flaws in its premises or its conclusions, and discarded it. His own long held answer was a negative one: the first book of *Genesis* had never been refuted. If he were alive today, he would be speculating skeptically the conclusion drawn from the not too recent experiment that passed an electric current through some inorganic elements and thereby produced amino acid. Did somewhere, sometime, on this planet just such a combination of circumstances occur, and life begin? Walter Chapin had the wisdom to know that man, despite all his learning, would most likely only in the hereafter breach the barrier guarding that secret of the universe. Perchance he at last knows the answer to the riddle of life.

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CASE RECORDS
OF THE
MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 42491

PRESENTATION OF CASE

A seventy-year-old woman entered the hospital because of abdominal pain.

Four months previously she noted intermittent episodes of vaguely localized, gnawing epigastric "hunger" pain that were unrelated to meals or time of day and not relieved by milk. The pain subsided when she stopped taking Serpasil, which she had been taking for fifteen months because of hypertension. One month before admission the pain recurred. It was more severe and occasionally radiated to the left side of the chest. One week before admission an upper gastrointestinal series demonstrated widened, thickened, tortuous and irregular folds throughout almost the entire mucosa of the stomach; no definite ulceration was seen; peristaltic activity was present; the pylorus opened readily, and a flexible retentive duodenal cap was outlined; the small intestine was normal. An abdominal film was normal except for scoliosis of the lumbar spine to the right. A barium-enema examination was negative. There was no melena, jaundice, nausea, vomiting or change in bowel habits. During the two months before admission she had lost 5 or 6 pounds in weight.

Physical examination showed a well nourished woman in no distress. There was no lymphadenopathy. The heart was not enlarged. One observer felt the lower edge of a mildly tender, movable epigastric mass that measured 4 or 5 cm. across. Another observer could not be certain of the mass.

The temperature was 98.6°F., the pulse 94, and the respirations 20. The blood pressure was 180 systolic, 100 diastolic.

The urine was normal. Examination of the blood revealed a hemoglobin of 13.2 gm. per 100 ml. and a white-cell count of 5100. The nonprotein nitrogen was 37 mg. per 100 ml. The fasting blood sugar, the bilirubin, the total protein and the amylase were normal. A gastric analysis revealed no free acid. Cytologic examination of the gastric fluid for malignant cells was negative. Three stool specimens were normal in color and gave negative guaiac tests. An upper gastrointestinal series (Fig. 1 and 2) demonstrated an oval mass that measured 6 cm. in maximum dimension in the posterior aspect of the greater curvature of the stomach; there was no tenderness in this region; the mass appeared to expand into the lumen of the stomach; the stomach was freely movable in this region; the mucosal folds, which were obliterated over the mass, were normal in the remainder of the stomach. A Graham test was negative. X-ray films of the chest demonstrated a small area of fibrosis at the apex of the right lung; pleural thickening was noted at the left apex; the heart was not enlarged, nor were the mediastinal and hilar lymph nodes.

An operation was performed on the second hospital day.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD SCHATZKI*: I assume that the operation was done on the stomach; at least that is what I am basing my discussion on. The case, as one reads the history, seems straightforward, but if one relies on the history alone one will be in for a surprise. I shall first discuss the appearance of the x-ray films that were given to me. The first set of films, taken outside this hospital, was reported to show diffuse thickening of the mucosal folds of the stomach. The picture of the stomach, with its numerous irregular filling defects, is weird. It is characteristic of foreign material in the stomach. This is what we see when a patient has disobeyed orders and has eaten a hearty breakfast before the gastrointestinal series is done. There is nothing that I can see that simulates thickened folds.

Some areas of the filling defects contain whorl-like structures; therefore, since this is a clinicopathological conference, I made sure that I could find no ascaris anywhere else in the intestinal tract. At times ascarides may completely fill the stomach and may be vomited up. Ascaris is rare in this part of the world and is highly unlikely to be present in such great numbers in the stomach without being visible in the small bowel. I do not see the whole small bowel, but what I can see looks normal, so that I think that ascaris can be dismissed. There is some foreign material in the stomach; I do not know whether it is food or something else. Along with the weird filling there is a constant ovoid filling defect.

The first examination at the Massachusetts General Hospital was done nine days after the examination done elsewhere and was a Graham test, which was not mentioned in the report. It demonstrates a normal gall bladder. The reason why I show it is that on one, and only one, of the films there is a peculiar

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line of increased density in the general position of the stomach. I cannot interpret it unless I assume that it is dye, which was retained for twelve hours in the

FIGURE 1. *Oblique View of the Stomach, with the Filling Defect in the Upper Portion of the Body (Arrows).*

stomach around the oval-shaped object. A film of the abdomen without contrast medium reveals nothing particular in the region of the stomach. The gastrointestinal examination done in this hospital ten days after the examination made elsewhere discloses that most of the filling defects in the stomach have disappeared and confirms my suspicion that ingested material — food or something else — was present previously. Again, the ovoid filling defect that was seen on the original films is present. It has remained in the same position as it was ten days previously; however, it does show some motion on several films. On one, the upper edge protrudes into the fundus, and on another, with the patient in the upright position, it has dropped down slightly. In the spot films the edge of the defect is nicely seen; the barium runs around it. The defect is smooth and is very sharply defined. The examiner apparently took films in various diameters and could demonstrate the ovoid defect at all times.

What could produce such a defect? The most obvious cause is a tumor of the wall of the stomach, arising either in the mucosa or below it. In favor of tumor is the fact that on a number of the films the mucosal folds seem to stop right at the edge of the defect. Also, over a period of fifteen days (there is a second examination that principally reveals the same findings), the mass has remained in approximately the same position. Several things, however, are difficult to explain by the presence of a tumor mass. Among these is the fact that it showed mobility. In one film it is in the upper part of the stomach (Fig. 1); in one of the later films it is tilted so that instead of lying up and down in the stomach it lies transversely in the lower part of the stomach (Fig. 2). A pedunculated polyp can show such mobility. As a matter of fact, it can show much greater mobility. Such a polyp can at times lie in the fundus of the stomach, and the same polyp at other times may be seen in the second portion of the duodenum. But a polyp with a stalk of that length would give some inkling of its presence on the films; I do not see any evidence of such a stalk. Furthermore, when such a pedunculated polyp moves, it usually pulls the stomach wall in, — it intussuscepts the stomach wall somewhat, — and the indented area in the wall can

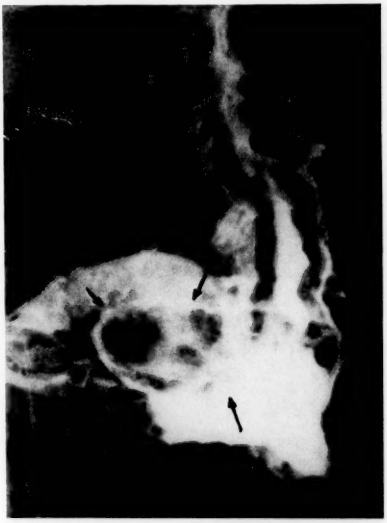

FIGURE 2. *Frontal Projection of the Stomach, with the Filling Defect Now Lying Distal to the Gastric Angle (Arrows).*

be seen. None of this is visible on any of these films so that I think polyp can be ruled out. Finally, the shape of the lower edge of the defect, which is not quite oval, but squared, is scarcely explainable by a tumor. On one film the edge of the mass is oval on one side and squared on the other.

I should like to ask a question that is not answered by the record; the answer will not influence my diagnosis. Was the patient mentally perfectly normal?

DR. BERNARD M. JACOBSON: Yes.

DR. SCHATZKI: I cannot conceive of any object of this shape and behavior that the human body has produced; I believe, therefore, that the mass was introduced by the patient. Whether it was introduced in its present size or whether as a smaller object that — like a trichobezoar — increased in size within the stomach, I have no right to say. On some of these spot films I have the impression of a vague structure to this mass with longitudinal lines, like grooves, on its surface. I have tried to decide what it might have been, but I cannot be specific about that. The reason I considered the possibility of a mental disturbance is that the patient had been taking Serpasil for quite a long time, and Serpasil may — I am told — lead to depression. Regardless of the answer to that question, I believe that this was a foreign body. This being a clinicopathological conference and since the mass obviously appears to have been a foreign body, I wonder if I missed an additional lesion that the surgeon operated on while incidentally removing the foreign body at the same time. I have to confess that I can see no other important abnormality. I have not mentioned the films of the chest because I see nothing in them that is exciting.

I believe, therefore, that this patient had a foreign body in the stomach.

DR. JACOBSON: During the first x-ray examination, done in a private office, when the patient was fluoroscoped the radiologist repeatedly asked her if she had eaten or drunk anything since the evening before. The patient vigorously denied eating or drinking anything at all. The physician repeated the questions after the next two x-ray examinations, and each time the patient denied eating or drinking anything before the examinations. Perhaps, that will influence you.

DR. SCHATZKI: It will not influence me in the slightest.

CLINICAL DIAGNOSES

? Gastritis.
? Lymphoma.

DR. RICHARD SCHATZKI'S DIAGNOSIS

Foreign body within stomach.

ANATOMICAL DIAGNOSIS

Foreign body within stomach.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The first operation was a gastroscopy. Dr. Benedict, will you tell us about that?

DR. EDWARD B. BENEDICT: I did the gastroscopy between the two x-ray examinations. Lying on the greater curvature of the stomach was a smooth, white mass, measuring 8 by 3 by 1 cm. in diameter, which I thought was a foreign body consistent with egg albumen or barium. I could not tell what it was.

DR. CASTLEMAN: It was not attached to the stomach?

DR. BENEDICT: No; but it could not be moved around much with the gastroscope. I took a biopsy from the mass and from the mucosa near it.

DR. CASTLEMAN: The biopsy from the mucosa showed slight chronic gastritis, and the biopsy from the mass showed amorphous material that was consistent with a foreign body, but we were unable to identify it. After the gastroscopy a second x-ray examination was done, and the patient was operated upon.

DR. CLAUDE E. WELCH: I thought that this patient had better be operated on because the foreign body had stayed in the stomach for a comparatively long time, and there might be an additional reason why it had remained there. Moreover, a mass of this size, if it passed into the intestinal tract, might cause trouble at a lower level, and certainly it could be more easily removed from the stomach than from anywhere else in the intestinal tract. Consequently, the patient was explored.

DR. CASTLEMAN: The foreign body (Fig. 3) was light green and contained a seed that looked like the

FIGURE 3

seed of an orange or a lemon, surrounded by material that looked like a pea pod or a string bean. I gather that there may well have been two foreign bodies together, the citrus-fruit seed and either a pea pod or a string bean. The mass was composed entirely of vegetable material.

DR. WELCH: We wondered whether we should send this specimen to Dr. Castleman or to the dietary department. We finally gave it to him. This falls in the group of cases that we call the "false-teeth" syndrome. The patient had begun using false teeth a couple of months before admission and had been swallowing her food without chewing it. She probably swallowed this material, which then accumulated in the stomach. Heretofore, we have seen this type of mass in the lower intestine after a subtotal gastrectomy as a result of orange pulp that has been ingested. It is of particular interest to raise the

question why the material did not pass through the stomach. I think the answer is that the pylorus was somewhat smaller than usual, so that it was difficult for such a mass to pass through it; in addition there was a great deal of gastritis that probably contributed. I was interested in knowing whether the Serpasil could have had any effect in suppressing the motility of the stomach and therefore in preventing emptying.

DR. JACOBSON: I do not think the dose of Serpasil did very much. The patient was never depressed. Also, the Serpasil was vomited at the onset of the abdominal pain four months before admission. I should call this the "no-teeth" syndrome rather than the "false-teeth" syndrome. She had had most of the teeth extracted about a month before the onset of symptoms. After the operation she told me that she was fond of chewing segments of navel oranges. She evidently was chewing a segment when it slipped down without her realizing it.

DR. CASTLEMAN: You think that the mass was composed of orange?

DR. JACOBSON: It was greenish yellow and had the yellow, fibrous coat of the navel orange.

CASE 42492

PRESENTATION OF CASE

A fifty-three-year-old shipyard foreman was admitted to the hospital because of melena.

Four years previously he was seen in the Out Patient Department because of weakness, fatigue and epigastric distress. There was a past history of alcoholism. Physical examination showed hepatomegaly. The bromsulfalein retention was 16 per cent. An upper gastrointestinal series demonstrated prominent gastric rugae and a small hiatus hernia. With a dietary regimen there was a gradual improvement in symptoms. Two years later he noted severe epigastric distress that was partially relieved by food and subsided after two or three months. An upper gastrointestinal series showed no change. One year before entry he again began to drink large amounts of alcohol. During the ten months before admission he lost 26 pounds in weight. Six weeks before entry he noted a persistent obstruction in the throat when eating that necessitated a gradual change from solid to soft and liquid food. Three weeks later persistent pain appeared in the right side of the face, neck and temporal region. Five days before admission there was an episode of "closure" in the throat so that he could hardly swallow or breathe. At about this time he was given antibiotic therapy for an infected tooth by a dentist. Later that day there were three episodes of coughing up of blood-streaked sputum and a subsequent episode of vomiting coffee-grounds material. There was no nausea. Swelling and tenderness of the right side of the neck were noted on the next day. He continued to cough up blood-tinged sputum and passed a tarry stool. On the day of admission he again passed a tarry stool.

Physical examination revealed a well nourished man with plethoric facies. Spider angiomas were present in the skin over the right clavicle. A Horner syndrome was noted on the right. There was hypal-

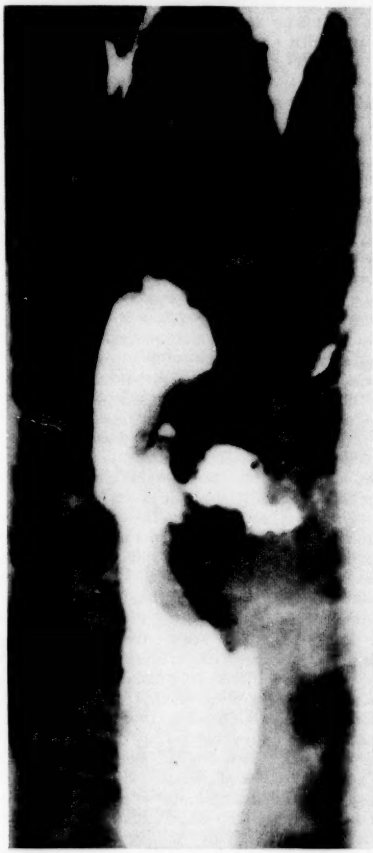

FIGURE 1. *Frontal Projection of the Barium-Filled Proximal Esophagus, Showing a Filling Defect at the Level of the Thoracic Inlet, with a Fistulous, Barium-Filled Tract Extending toward the Left.*

gesia of the right side of the face. The right side of the neck was swollen, tender and crepitant. The trachea was in the mid-line. The thyroid gland, which was not enlarged, was diffusely tender. The teeth were carious. Laryngoscopic examination

demonstrated a mass pushing the epiglottis slightly to the left; the vocal cords moved normally. Examination of the heart revealed a Grade 2 apical systolic murmur. The edge of the liver, which was firm, was felt 2 fingerbreadths below the right costal margin. The spleen was not palpable. Rectal examination was negative.

The temperature was 99.2°F., the pulse 64, and the respirations 24. The blood pressure was 128 systolic, 78 diastolic.

The urine gave a ++ test for albumin. Examination of the blood revealed a hemoglobin of 10.6 gm. per 100 ml. and a white-cell count of 11,000, with 73 per cent neutrophils. The nonprotein nitrogen was 23 mg., the bilirubin 0.4 mg., and the total protein 6.9 gm. per 100 ml. The amylase was 3 Russell units. The alkaline phosphatase was 8.8 units. The prothrombin content was 26 per cent. The cephalin flocculation was ++. The thymol turbidity was 1.5 units, with a negative flocculation. The bromsulfalein retention was 14 per cent. A stool specimen was tarry and gave a ++++ guaiac test. An upper gastrointestinal series demonstrated a filling defect that measured 5.5 cm. in length and about 2 or 3 cm. in width in the proximal portion of the esophagus at the level of the suprasternal notch; barium extended from a large central ulceration in the filling defect into the soft tissues of the neck on the right; the outer edge of the filling defect suggested a smooth contour (Fig. 1); the mediastinum was widened from the level of this lesion to the pulmonary hilus on the right; there was a suggestion of an esophageal varix. X-ray films of the chest were normal except for the changes in the esophagus and superior mediastinum. Films of the neck demonstrated a fullness of the soft tissues, with several small air pockets in the lower portion of the right side. Sigmoidoscopic examination was negative.

Esophagoscopic examination showed an obstructing, firm, smooth, gray mass, 1 cm. below the cricopharyngeus muscle. A biopsy specimen revealed normal esophageal tissue. The patient continued to cough or spit up blood-streaked sputum, and the stool specimens continued to give ++++ guaiac tests. On the fourth hospital day he became sweaty and cold and collapsed. The pulse was weak and thready, and the blood pressure fell to 50 systolic, 30 diastolic. After a transfusion of blood, the blood pressure rose to 110 systolic, 70 diastolic, and he felt better. On the next day the temperature rose to 105°F. The hemoglobin was 9.7 gm. per 100 ml., and the white-cell count was 33,600, with 85 per cent neutrophils. A blood culture showed no growth. With aspirin therapy and an alcohol sponge bath the temperature fell to 102°F. On the sixth hospital day there was a sudden massive hematemesis, consisting of bright-red blood, which the patient aspirated. Despite a tracheostomy he died shortly thereafter.

Differential Diagnosis

Dr. Warren Point*: May I see the x-ray films?

Dr. Paul M. G. St. Aubin: The gastrointestinal study at the time of the episode four years before admission shows a relatively normal-looking stomach. Prominent folds were described at that time; I assume that they were better seen at fluoroscopy. At the time of admission a gastrointestinal study, which included the upper end of the esophagus, was done. The pyriform sinuses are overfilled with barium. The esophageal orifice is small. In the cervical esophagus there is a rounded, smooth, filling defect in the center of which is a hole and a passage filled with barium, extending into the soft tissues adjacent to the esophagus (Fig. 1). The superior mediastinum seems to be widened, and the barium extends up into the soft tissues of the neck and anteriorly into the superior mediastinum from the esophageal lesion. The lateral and anteroposterior films of the neck show a marked widening of the retropharyngeal space and bubbles of gas in the soft tissues, extending from the level of the perforation in the mass to the level of the styloid process at the base of the skull. There is obviously swelling of the soft tissues in the lateral aspect of the neck. The plain transverse film of the abdomen reveals that the liver extends down to the level of the iliac crest, and the right leaf of the diaphragm is in relatively normal position; the spleen, on the other hand, appears to be of normal size. The protocol states that a question of varices was raised. In the spot films of the esophagus there is a small hiatus hernia and possibly a filling defect here, but I am not convinced that there are varices. Would you look at the films, Dr. Schatzki, and tell us what you think?

Dr. Richard Schatzki: I should say that there is not sufficient evidence for one to call these varices.

Dr. Point: I should like to discuss first the possible cause of death. Obviously, the patient died because of hemorrhage and aspiration of blood into the lung. I think I can pin down the bleeding to the gastrointestinal tract, since he had melena and also vomited blood in large quantities and since on one occasion he went into shock and was improved by blood transfusions. A number of "red herrings" present themselves. Several years before admission he had been an alcoholic; he had an enlarged liver and an increased bromsulfalein retention. There were also said to be varices, but I am willing to believe that he had no appreciable varices. I think it is worth while to point out, however, that there is increasing evidence that varices may be present and may be seen only during esophagoscopy. At any rate I do not believe that the varices were important enough to cause significant bleeding unless there was a perforation into a varix. The lesion in which perforation would most probably have occurred was high

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in the esophagus. Unless there were large varices below that level I doubt if large varices would be present high in the esophagus.

There were enlarged gastric folds, which is a finding consistent with gastritis. We know that gastritis may bleed sometimes. I cannot say that the patient had gastritis on the basis of the x-ray films alone. He may well have had alcoholic gastritis, but I do not believe that the gastritis contributed a great deal to the massive bleeding.

Then, too, there was an episode suggestive of an ulcer. The severe epigastric pain relieved by food makes one wonder about duodenal ulcer. I doubt if I need to assume an ulcer. He had a small hiatus hernia, which, of course, can bleed excessively at times. I shall discard that possibility.

I believe that the source of the bleeding was most probably an ulcerated tumor lying high in the esophagus and was the lesion that is most dramatically demonstrated in the x-ray film.

The first symptom was dysphagia, which in the great majority of cases of esophageal tumor does appear first, without nausea, pain or malnutrition. Patients with esophageal tumors characteristically describe to the physician, unfortunately months after the onset, a sense of a lump in the throat, food not passing down quite well or a mild discomfort after swallowing solid foods. Although there was rapid progression of the course from the onset of dysphagia six weeks before entry, I think the findings do fit a tumor of some kind quite well. Moreover, a tumor is visible in the x-ray films. Was this necessarily a primary tumor of the esophagus, or could it have been a metastasis? The first metastatic tumor I should consider is one from the gastrointestinal tract. There was no evidence for that, however. Tumors in this region most commonly arise from the thyroid gland, the larynx or the upper esophagus. The thyroid gland was stated not to be enlarged and was palpable, so that I shall dismiss that as a source of tumor. The laryngoscopic examination revealed normally functioning vocal cords although there was a mass pressing upon the epiglottis. I assume, however, that these masses pressing exteriorly upon the laryngeal structures could well have been associated with the tumor that was visible below that area.

One metastatic tumor comes to mind — that is, a metastasis from a hepatoma, arising in an alcoholic cirrhotic liver, but there is no real proof that the patient had cirrhosis and no proof that he had a hepatoma, either. The liver was described as being only 2 fingerbreadths below the right costal margin, in spite of the fact that the x-ray films demonstrated a much larger liver. I shall assume that the liver was probably not tremendously enlarged and shall accept the opinion of the radiologist that the spleen was of normal size. Also, the liver-function tests did not indicate a great deal of cirrhosis. The one finding in favor of that diagnosis was the spider angiomas over the clavicle. If they were present, I have to give serious consideration to chronic liver disease and, hence, presumably, to cirrhosis. In the absence of varices and of an enlarged spleen, however, I shall not emphasize that point. A primary carcinoma arising in the trachea or the bronchial passages could penetrate the esophagus, but because of the onset and the course of the disease I am inclined to call it primary in the esophagus.

What kind of tumor could it have been? The most frequent primary tumor of the upper esophagus is squamous-cell carcinoma; adenocarcinomas usually occur in the region of the esophageal gastric junction. I must also consider sarcoma, but sarcoma of the upper esophagus is an extremely rare disease; it is said to occur in about the ratio of 1:150 compared to squamous-cell carcinoma. Lymphoma or a similar malignant process may have been present, but there were no enlarged lymph nodes peripherally, no enlarged spleen and no appreciable fever before admission.

The question also arises, Could this have been a foreign body? It is conceivable that the patient swallowed a fish bone or perhaps a toothpick. A toothpick may penetrate the gastrointestinal tract and form a large abscess. I am inclined somewhat against this diagnosis by the course of the disease. There was no appreciable fever before the terminal phase in the hospital; the white-cell count on admission was only 11,000, and the differential count was not in favor of massive sepsis. I do not believe, therefore, that this was in the very beginning, at least, a foreign-body perforation of the esophagus. As the patient approached the terminal phase, obviously, an abscess formed; there was diffusion of gas, air and pus up through the tissue planes of the neck and down into the mediastinum. It is not rare to find a perforation of the esophagus into any structures of the mediastinum, or neck, with carcinoma. It may penetrate the pericardium, the pleural cavity and, occasionally, even the aorta. Of course, in the latter event the terminal phase is massive hematemesis, as it was in the patient under consideration. I do not believe that the aorta was involved because the perforation was too high. Is that not true, Dr. St. Aubin?

DR. ST. AUBIN: I should think it was unlikely from the location of the barium extending from the esophagus into the superior mediastinum.

DR. POINT: It is conceivable.

DR. ST. AUBIN: It is possible that some of the branches of the aorta on the right side could have been involved.

DR. POINT: It is possible but not likely. Massive hematemesis, melena and shock are found in about 3 per cent of patients with esophageal carcinomas — in fact, melena rarely may be the first symptom. Dysphagia is by all means the most common early symptom. I should therefore like to reconstruct the picture by saying that the patient undoubtedly had

chronic alcoholism and, possibly, a mild cirrhosis of the liver, although I do not believe that cirrhosis of the liver played an important part in the final episode. Gastritis was probably present because he was an alcoholic. The hiatus hernia was an incidental finding, a "red herring," one might say. The important disease was squamous-cell carcinoma of the upper end of the esophagus and, I suspect, involvement of a large portion of the neck structures and the mediastinum, possibly by local spread of the carcinoma. Also, one might assume that the Horner syndrome was caused by stellate-ganglion involvement; and the trigeminal-nerve involvement may well have been caused by the dissection we see, but more probably resulted from the spread of the carcinoma up within these tissue spaces to involve the neurologic structures. There was also widening of the mediastinum, with abscess and mediastinitis. There may well have been involvement of the venous structures of the neck. I was impressed by the plethoric appearance of the patient, in spite of the fact that he had a hemoglobin of 10.6 gm. per 100 ml., and I wondered if this could have been a superior-vena-cava syndrome with compression of the superior neck veins, if not the vena cava itself. He apparently demonstrated no enlargement of the vessels of the forehead. I suspect that he had a tracheoesophageal fistula, which was the reason for his coughing up blood, having choking spells and so forth. The final episode was undoubtedly produced by massive hemorrhage from some larger blood vessel, possibly a vein or a major artery or, less likely, from esophageal varices and aspiration of the blood, with pneumonitis, atelectasis and death.

DR. BENJAMIN CASTLEMAN: Dr. Schatzki, would you comment on the x-ray findings and the possibility of tumor?

DR. SCHATZKI: I think that the x-ray appearance is quite surprising for any tumor, but an abscess is apparently ruled out by the clinical findings. This could have been a primary carcinoma of the cervical esophagus; but if I had to choose, in spite of the fact that a primary carcinoma of the cervical esophagus is more common than any other tumor, from the appearance of one of the spot films I should believe that this was one of the rare tumors of the esophagus, like leiomyosarcoma, or involvement of the esophagus from the outside by tumor.

DR. ST. AUBIN: Are you basing that opinion on the fact that the defect has a smooth wall?

DR. SCHATZKI: Yes; on the smooth wall and the small central area of ulceration.

DR. CASTLEMAN: That was also suggested by the members of the Department of Radiology preoperatively.

DR. EDWARD B. BENEDICT: At the time of the esophagoscopy I thought that this was a primary carcinoma of the esophagus, but in retrospect there are several findings against it. It looked smooth, and the biopsy was negative although I had thought I removed an adequate piece. Furthermore, in the history there was a constant complaint of blood-streaked sputum, which could well have come from a primary

FIGURE 2. *Photograph of the Esophagus. Arrow points to the carcinoma of the esophagus, with a fistulous opening.*

carcinoma of the bronchus, with metastases to the neck and extrinsic invasion into the esophagus.

DR. ALFRED KRANES: Do you remember a similar case, without evidence of a tumor, in which twice biopsies taken at esophagoscopy were negative? That tumor was also smooth.

DR. BENEDICT: I agree with Dr. Kranes that it is possible but unusual not to get a positive biopsy in cancer of the esophagus. In the cases to which he refers I did two esophagoscopies, and although both times I saw the lesion and thought it was carcinoma, the tumor was so small and soft that I was unable to get positive tissue; however, at the first attempt in

that case the pathologist reported, "atypical cells, which may be carcinomatous."

DR. CASTLEMAN: Dr. Schatzki, would you look at the films of the stomach and duodenum and tell me if you can see any abnormality? Is there a duodenal ulcer?

DR. SCHATZKI: Yes; there could be an ulcer almost in the second portion about 2.5 or 3 cm. from the pylorus. If that is not the ulcer, I cannot see it.

CLINICAL DIAGNOSIS

?Lymphoma of right side of neck, with fistulous tract.

DR. WARREN POINT'S DIAGNOSES

Squamous-cell carcinoma of esophagus, with mediastinal extension and tracheoesophageal fistulas.
Massive hemorrhage into gastrointestinal tract from eroded vessel by tumor.
Aspiration pneumonia and atelectasis.
Cirrhosis of liver, alcoholic type.

ANATOMICAL DIAGNOSES

Squamous-cell carcinoma of cervical esophagus, with fistulous tracts into neck and with extension into trachea.
Bleeding duodenal ulcer, with massive gastrointestinal hemorrhage.
Cirrhosis of liver, alcoholic type.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The cause of the sudden death was hemorrhage from a duodenal ulcer. There was a good-sized, very active chronic duodenal ulcer.

DR. SCHATZKI: Can you remember how far the ulcer was from the pylorus?

DR. CASTLEMAN: It was just beyond the pylorus.

DR. SCHATZKI: Then the shadow that I pointed out was not the ulcer and I cannot see it.

DR. CASTLEMAN: The stomach and the entire gastrointestinal tract were filled with fresh blood. Here is the specimen of the esophagus (Fig. 2). There was a fistulous opening, about 3 by 2 cm., which extended over to the right, producing a very large abscess filled with pus and very little blood. There is good evidence, therefore, that the bleeding was not coming directly from this area, although there was no reason why it should not have. The edge of the lesion was hard, and in the gross we believed that it was a primary carcinoma of the esophagus. It extended into the trachea, forming a tiny, white nodule, but there was no ulceration of the trachea. Microscopically, the tumor was a squamous-cell cancer, with infection along with it.

DR. KRANES: One point worth stressing is that massive bleeding from a carcinoma of the esophagus at such a high level would be likely to produce more vomiting of blood. The fact that the initial hemorrhage was not manifest should have led to the suspicion that the source of bleeding was lower down.

DR. CASTLEMAN: There was a fairly severe alcoholic cirrhosis of the liver, which weighed 2000 gm. and extended, at the time of death, 3 fingerbreadths below the right costal margin; it may have extended 6 fingerbreadths below the costal margin during life. We found no esophageal varices, although we examined the esophagus carefully. The spleen was not enlarged.

A PHYSICIAN: Was there a direct communication between the esophagus and the bronchus, or was the blood aspirated?

DR. CASTLEMAN: There was some aspirated blood in the bronchus at autopsy.

DR. POINT: It is said that with esophageal carcinoma there may be enough overflow of the secretions to cause a tracheitis at times.

DR. CASTLEMAN: I think there was an overflow of the blood from the stomach.

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ANOTHER DAY OF RECKONING

FIFTY years ago the first Food and Drug Act was passed into law by Congress, and it is a tribute to the Food and Drug Administration that the particular abuses that the Act was originally designed to correct have passed into the unreality of history. The vapor cure for consumption, the use of glycerine lotion for the treatment of diphtheria and erysipelas, the vegetable cancer cure, brain food for "nervous debility" — all these patently absurd nostrums seem almost benign and even humorous from the perspective of five decades. And yet if they were retold, the stories of the cancer and tuberculosis victims who were duped by the advertising claims of such patent medicines would have lost none of their genuine pathos and capacity to arouse righteous indignation.

It is of interest that the first general food law was passed in Massachusetts in 1784. However, not until 1906 did Congress, under the pressure of public opinion, pass the law designed to end a patent-medicine era of "caveat emptor" and replace this principle with one of "Public interest comes first."

After Theodore Roosevelt signed the act, factory conditions improved, laboratories were set up to test samples of foods and drugs, and labels were changed to declare chemical preservatives used in processing foods, and to give consumers information for intelligent purchasing. Between 1906 and the present a number of amendments were added to the original act that strengthened it and supposedly put teeth into enforcement provisions. Notable among these were the Copeland Bill (1938), completely revising the first Food and Drug Act, and the Durham–Humphree Amendment (1951) that specifically prohibited dispensing of certain dangerous drugs without a doctor's prescription.

Hence, it might appear that a brave new world of enlightenment regarding foods and drugs has emerged. Unfortunately, this is far from the fact. Moreover, many of the teeth of enforcement have become broken. In recent years the greedy proponents of "caveat emptor" have become more powerful, more subtle and, if anything, more vicious. Instead of Pettit's eye salve ("if it don't open within ten days, send for a box of it") and Dr. Thomas's electric oil ("restored a crooked limb with six applications"), the physician and the consumer are now deluged with a flood of preparations, properly labeled to be sure, but accompanied by quasi-scientific pamphlets filled with a sophisticated version of the double talk used so effectively by the traveling medicine men of a bygone era. "Allen's Brain Food" has its modern counterparts in geriatric mixtures, purporting by nutritional means to reverse senility. "Red clover blossoms," a "blood purifier" of the past, yielded to a preparation that claimed to remove fatigue from "tired blood." Expensive vitamin preparations that are supposed to contain mysterious life forces obtainable only from compost heaps are currently sold from door to door.

Garlic is still marketed as a potent antibiotic (better than penicillin), and the descriptive literature about a certain vitamin preparation has suggested that it effectively prevents poliomyelitis. Many producers of such products, with arrogant hypocrisy, list on the packages or in the accompanying brochures obscure and discredited research studies to support their claims. This is the ammunition with which to fight law enforcement. For example, test-tube experiments suggesting that extract of garlic can destroy bacteria are cited to support the idea that garlic pills may be useful in the treatment of active tuberculosis.

Every physician is all too familiar with the extravagant claims made for too high a proportion even of the generally ethical pharmaceuticals, samples of which are found in his mail box each day. Although they are habitually discounted, such claims and the atmosphere of exaggeration and distortion that lie behind their advancement and their reception provide the perfect smoke screen for the nostrum manufacturer to market his modern brand of snake oil with impunity. The whole atmosphere created by exaggerated advertising claims is so often unhealthy that it cannot help disturbing the pharmaceutical industry as a whole.

In 1955 the Food and Drug Administration, now a part of the Department of Health, Education and Welfare, was facing, with its 1940 staff and reduced budget, a great expansion in population and in the volume of production reaching the consumer, a host of new products such as frozen and ready-to-serve foods, as well as thousands of new drugs manufactured by new processes and containing new ingredients. It was obvious that the job of the Food and Drug Administration had grown far too big for its facilities. Accordingly, a citizens' committee was appointed to study the adequacy of the Administration programs and to make appropriate recommendations. The Committee delivered its report last June and recommended a substantial increase in the Administration's staff and facilities and in its educational activities.

The physician is among those best qualified to recognize the urgency and importance of supporting these recommendations. More than that, on the fiftieth anniversary of the Administration, physicians are well aware that a real need continues — it has actually increased — for the co-operation of the medical profession in offering expert medical testimony on behalf of the Government in its contested actions. It is only through such co-operation that the Food and Drug Administration is able to implement the provisions of the law designed to safeguard the public against misbranded or dangerous drugs and devices — in short, to repair its broken teeth.

The purveyors of quack drugs today are formidable adversaries, adept in the use of scientific jargon and the manipulation of half truths, and possessed of experience, organization and funds. It will take the vigilance and ingenuity of the medical profession working in co-operation with the Food and Drug Administration to meet the continuing problem in its new guise, which presents as much of a challenge now as it did fifty years ago.

A DOCTOR'S HAPPY LIFE

Dr. Roger Irving Lee, of Boston, three score and ten and beyond and bluntly sagacious, as is his nature, has taken a long look into his rear-view mirror and produced a medically historical philosophic autobiography. Philosophical he would call it, rather than philosophic, but that is because he refuses to make concessions to noncontributory changes whether in manners, morals or literary customs. The book that he has written under the engaging title "The Happy Life of a Doctor" is published by Little, Brown and Company, also of Boston, and is so fresh off the press as barely to have reached the booksellers' stalls.

In whatever field he has entered, Roger Lee has been a dominant figure because of his ability to grasp the facts of any situation a little sooner than the run of mankind, and because of his courage in hewing to the line regardless of general officers, university presidents or other consequences, but in particular regardless of intellectual or scientific pretentiousness on the part of anyone. "The Happy Life of a Doctor" is a frank and unbuffed account of his professional activities and achievements and of his personal life, and a clear statement of his conclusions on a variety of subjects from the universality of medicine to the folly of compulsory retirement on account of age.

One of the coming young physicians of Boston in the first decade of the century, with an appreciation of the value of medical research and an understanding of its technics, Roger Lee was called at the age of thirty-three to become the first Henry K. Oliver Professor of Hygiene at Harvard College. He left the post in the following year to serve through most of World War I, first with the British and then with the American Expeditionary forces, returning to a somewhat disrupted academic milieu as a lieutenant colonel — a title that he shed as soon as he could find a suit of civilian clothes that fit.

He continued his professorship until 1924, serving also during the last year of his academic career as temporary dean of the new Harvard School of Public Health, which he had helped to create. His resignation in order to re-enter private practice was opposed by President Lowell, on the ground that at forty-two Dr. Lee would be unable to make a living on the common level. This was perhaps the only uncautious misstatement of Mr. Lowell's long and illustrious career.

Dr. Lee recounts some but by no means all of the honorable responsibilities with which his life has been singularly charged, in addition to that of a successful consulting practice; the presidency of the Massachu-

setts Medical Society and of the American Medical Association, and the one-time chairmanship of the committee of the Society that holds this journal in its care; his election in 1930 as an overseer of Harvard, and in the following year as a fellow of the Corporation, a post that he held with unique distinction until his resignation in 1953.

In conclusion he lists not entirely facetiously a number of the possible epitaphs that might appropriately be carved at some distant time upon his tombstone. They end with the one that could well express his own simple preference:

> Or may be on my tombstone I am only going to have "Doctor." And perhaps just "Doc."

TUBERCULOSIS CONTROL, NATIONAL AND LOCAL

In spite of the notable advances in control since the first Christmas Seal Campaign was conducted by the National Tuberculosis Association in December, 1907, tuberculosis remains a major threat to the health of the American people. With a third of the nation's population positive reactors to tuberculosis an obvious source of infection exists. Great progress has been made in the saving of lives of tuberculous patients, but serious problems of prevention and control remain. Approximately 100,000 new cases occur each year, and at present, there are 400,000 active cases of infectious tuberculosis, 150,000 of these unreported to health authorities. If the present rate of breakdowns continues among those infected with the tubercle bacillus, it is estimated that 2,700,000 will be afflicted with active tuberculosis during their lifetime.

Today, there are approximately 800,000 patients with tuberculosis that has been converted from active to inactive, and to assure complete recovery, it is necessary to provide not only satisfactory medical treatment and supervision but also help for emotional and economic problems. The annual Christmas Seal Campaign, which began on November 16 and will continue through December, has been an essential part of the national effort at control of tuberculosis. To support preventive programs of health education, case finding, rehabilitation and medical and social research, large sums must be raised in each yearly campaign. The national cost of tuberculosis is $600,000,000 a year, largely in tax dollars, and there are 1,200,000 patients who require medical care or supervision. Against this enormous sum, the amounts contributed in each Christmas Seal Campaign seem modest indeed.

Even as the broad interests of tuberculosis control are being thus served it is important to note that in the local area a greater degree of autonomy has been decided on. With the highest death rate from tuberculosis of any large city in the country occurring in Boston, the Boston Tuberculosis Association has found it necessary this year to separate itself from the state and national associations and carry on its own seal sale with its own seal.

Conducting as it does highly effective activities in the way of education, slum improvement and diagnostic facilities, as well as a sheltered workshop and a preventorium, the members of the Boston Association believe that it can no longer bear the burden of having an increasing proportion of its funds diverted to the state and national organizations. This now amounts to 14 per cent of the proceeds of the seal sale, and a recent ruling of the national association calls for the payment to it of 6 per cent of all gifts made to the Boston group.

The Boston Association is consequently making its independent plea for funds, all of which will be used in its own area.

STANDARDIZATION OF ATARACTIC AGENTS

An expressionless mask, it is said, appearing like a drawn curtain to hide the animated features characteristic of man in his more conscious moments has become a recognizable physical entity in many of the places where men congregate. The withdrawal of the personality from active participation in the emotional experiences of mankind that this ubiquitous lack of expression is taken to indicate is supposed to result from a mass addiction to those pharmacologic products to which a tranquil state of mind is now generally attributed.

The use of these psychotherapeutic agents having reached such proportions, both here and abroad, some simple and inexpensive method of biologic standardization on a behavioral level has seemed desirable. For these experiments an approachable and easily handled, yet sufficiently excitable semidomesticated animal was necessary. The larger zoologic specimens such as the lion (*Felis leo*) and the rhinoceros (family Rhinocerotidae), although excitable, were eliminated for practical reasons; the hippopotamus (*Hippopotamus amphibius*) because of its large size and natural tranquillity; the shrew (family Soricidae) because of its small size and relative inaccessibility.

At this juncture Walaszek and Abood,* of the departments of Psychiatry and Biochemistry, University of Illinois College of Medicine, made their own brilliant contribution to the solution of the problem. The Siamese fighting fish, *Betta splendens,* although not customarily considered a prey to anxiety, is naturally

*Walaszek, E. J., and Abood, L. G. Effect of tranquilizing drugs on fighting response of Siamese fighting fish. *Science* 124:440, 1956.

and consistently pugnacious and will fight fiercely, though silently, whenever confronted with a homologous opponent. The characteristic fighting stance of *B. splendens,* according to these authors, involves the expansion of the pectoral fins and branchial membranes, followed by a vicious, mutual frontal attack, often resulting in the death of one combatant or the other.

A special rectangular aquarium was accordingly devised, separated into two chambers by a watertight transparent Lucite bulkhead and a removable opaque panel. The drug under study was dissolved in the chamber containing the experimental fish; after the fish had been sufficiently exposed the opaque panel was removed, he was brought into view of the normal fish in the other chamber, and his reactions observed.

A variety of drugs were thus investigated: three so-called tranquilizing agents (reserpine, meprobamate and chlorpromazine); a detoxification product of chlorpromazine; three antihistaminics, one with sedative action; a brace of hypnotics; an analgesic, and a drug with combined sedative and analgesic properties. The results were interesting and perhaps momentous.

Whereas under the influence of hypnotics, sedatives and analgesics the fish retained their fighting propensities, both tranquilizers and antihistaminics produced in every case more or less depression and a complete blocking of the fighting response accompanied by a phenomenon of backing water that propelled them hastily to the rear. In the words of a recent political utterance they faced the future by retreating backward into the past. As to the action of the quondam fighters under the influence of the antihistaminics, "another peculiarity was that they became pale upon exposure to a control fish exhibiting the fighting response." If such a reaction cannot be described as showing the white feather it must at least have some parallel significance in reference to the scales.

In the quiet search for global tranquillity, similar experiments on the Russian red snapper and the Chinese swordtail are in order, which, if successful, may result in the development of huge pharmaceutical markets in the heartlands of Europe and adjacent continents.

Hygiene of Dress — *In summer we discoursed upon* hoops, *as pleasantly administering to the cooling of the heated body, and we now believe it our imperative duty to reiterate the warning then prompted by our interest in the welfare of the gentler sex, and to say, beware of extremes in their circumference* — "don't take cold"!

Boston M. & S. J. *December 11, 1856*

MASSACHUSETTS MEDICAL SOCIETY

TOXIC HAZARDS*

Methyl Chloroform†

In an earlier article, the hazards in the use of carbon tetrachloride were pointed out, and trichlorethylene was discussed as a safer substitute. In recent years another substitute also has appeared. Known as methyl chloroform, or 1,1,1, trichlorethane, it is prepared by chlorination of ethyl chloride. With the formula CH_3CCl_3, methyl chloroform should be distinguished from the time-honored anesthetic chloroform (trichloromethane), which has the formula $CHCl_3$.

Methyl chloroform is a colorless, volatile solvent with a pleasant odor. It is slightly toxic and nonflammable. This solvent can be used as a substitute for carbon tetrachloride. It will do practically every cleaning job that carbon tetrachloride can do and is much safer to use. To compare their toxicities, the Commonwealth of Massachusetts has set up a maximum allowable concentration of 25 parts per 1,000,000 parts of air for carbon tetrachloride and 250 parts per 1,000,000 parts of air for methyl chloroform. These allowable concentrations are, of course, based on a continued exposure for an eight-hour day.

Methyl chloroform has many uses, such as cleaning of printing type, generators and electric equipment and numerous other cleaning operations.

Like all solvents, it is toxic in the sense that it can cause acute and chronic poisoning under certain conditions. Acute poisoning will result from inhalation of high concentrations, and the chief effect is as an anesthetic to the central nervous system. Chronic poisoning can be caused by this solvent, although it occurs rarely and only if the worker has been exposed continually to concentrations that would produce symptoms of acute poisoning. It is relatively nontoxic to the kidney and liver, whereas, as is well known, carbon tetrachloride is a strong liver and kidney poison.

Methyl chloroform is not readily absorbed by the skin. However, it can cause dermatitis by repeated

*This is one of a series of articles published co-operatively by the Committee on Industrial Health and the Panel on Child Health of the Committee on Public Health of the Massachusetts Medical Society. The panel provides liaison with the Massachusetts Chapter of the American Academy of Pediatrics, whose Boston and Worcester Poison Information Centers are activities of the Committee on Accident Prevention.

†From the Committee on Industrial Health, George F. Wilkins, M.D., *chairman;* Henry C. Marble, M.D.; Karl T. Benedict, M.D.; Harriet L. Hardy, M.D.; George E. Morris, M.D.; Albert O. Seeler, M.D.; and Jermyn F. McCahan, M.D.

contact with the skin owing to its defatting action. If the vapors come in contact with the eye, they can cause eye irritation.

There are certain cases in which methyl chloroform is used as a spray. When it is used in this manner, goggles and an airline respirator should be worn by the worker to prevent eye irritation and the anesthetic action. Anyone employing this solvent in the form of a spray should have the worker under constant supervision, and, at the appearance of any symptoms of an anesthetic nature, the worker should be removed immediately to the fresh air.

The general trend today is for more and more manufacturers to recommend and incorporate methyl chloroform into their cleaners and even to go so far as to state that they are manufacturing the solvent as a substitute for carbon tetrachloride.

BENJAMIN P. W. RUOTOLO
Massachusetts Division of Occupational Hygiene

DEATHS

FINN — Herbert G. Finn, M.D., of Boston, died on November 13. He was in his fiftieth year.

Dr. Finn received his degree from Harvard Medical School in 1932. He served on the staffs of Carney, St. Elizabeth's, Sancta Maria and Lawrence Memorial hospitals, Boston, and the Danvers State Hospital, Danvers, and the Holy Ghost Hospital, Cambridge, and Soldiers Home, Chelsea. He was a fellow of the American Medical Association and the American College of Surgeons, a committee member of the American Cancer Society and a member of the Industrial Medical Association.

He is survived by his widow, five daughters and three sons.

LAKEMAN — Mary Ropes Lakeman, M.D., of Salem, died on June 26. She was in her eighty-sixth year.

Dr. Lakeman received her degree from Boston University School of Medicine in 1895. She was a former director of the Division of Child Hygiene, Massachusetts Department of Public Health, trustee and board member, New England Home for Deaf Mutes, secretary of the Association for Women in Public Health and its president for three years, a retired fellow of the American Medical Association and a member of the Massachusetts Home Medical Society, American Public Health Association and the American Child Health Association. At sixty-seven, she held a post with the women's field army of the American Cancer Society where, for five years, she taught women to recognize cancer in its earliest stages.

She is survived by a grandnephew.

CORRESPONDENCE

MORTALITY WITH COMMON-DUCT STONE

To the Editor: It has been called to my attention that there is an error in the review of "Biliary Surgery" by Dr. Cattell and myself in the October 11 issue of the *Journal*. The error, which was entirely ours, is at the top of page 703 and concerns the following sentence: "Further analysis of the records of 435 patients who had combined cholecystectomy and choledochostomy shows that there were 3 deaths in 119 patients with common-duct stones, a mortality of 2.5 per cent, and 2 deaths in 216 patients in whom the common bile duct was explored but no stones were found." This should have read, "and 2 deaths in 316 patients in whom the common bile duct was explored but no stones were found." The mortality in this group of patients with negative exploration of the common duct should have read 0.6 per cent rather than 1 per cent.

The correction of this statistical error fortunately does not alter the conclusion that we drew from this analysis; rather, it tends to strengthen it in the sense that the mortality in the group of patients who had combined cholecystectomy and choledochostomy and in whom no stones were found in the common duct was actually less than that for cholecystectomy alone.

KENNETH W. WARREN, M.D.
Boston

BOOK REVIEW

Sexual Precocity. By Hugh Jolly, M.D. (Camb.), M.A., M.R.C.P. 8°, cloth, 276 pp., with 69 illustrations and 5 tables. Springfield, Illinois: Charles C Thomas, 1955. $6.75. (Publication No. 200, *American Lecture Series.*)

The first section of this monograph presents the definition and classification of sexual precocity, with a discussion of etiology, pathological physiology, prognosis and therapy. There is a review of the literature of historical interest.

The second section gives brief case histories, most with photographs, of 69 cases of precocity.

This large series of a relatively infrequent and mystery-surrounded phenomenon is of great value. The classification is clear, and the pitfalls of diagnosis and treatment are well presented.

The discussion of pathological physiology is inadequate particularly in the adrenogenital syndrome. The bibliography includes only 4 references later than 1950, a reflection, no doubt, that the monograph was originally a thesis for the degree of Doctor of Medicine (given in 1951).

ROBERT L. NIELSEN, M.D.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Head Injuries and Their Management. By Francis Asbury Echlin, M.D., C.M., M.Sc., Med. Sc.D., professor of clinical neurosurgery, New York University Postgraduate Medical School, neurosurgeon, Lenox Hill Hospital, attending neurosurgeon, Bellevue Hospital and New York Eye and Ear Infirmary, and consulting neurosurgeon, St. Luke's Hospital, Newburgh, and Kingston Hospital. 12°, cloth, 127 pp., with 10 illustrations and 1 table. Philadelphia: J. B. Lippincott Company, 1956. $3.00.

Emotional Hazards in Animals and Man. By Howard S. Liddell, Ph.D., professor of psychobiology and director of the Behavior Farm Laboratory, Cornell University. 8°, paper, 97 pp. Springfield, Illinois: Charles C Thomas, 1956. $2.50. (Publication No. 299, *American Lecture Series.*)

Tribute to Freud. By H. D. 8°, cloth, 180 pp., with unpublished letters by Freud to the author. New York: Pantheon Books Incorporated, 1956. $2.50.

Kinderärztliche Notfallfibel: Abwehr akuter Lebensbedrohung. By Prof. Dr. B. de Rudder, director, Univ.-Kinderklinik, Frankfurt A.M. Third edition. 8°, cloth, 178 pp., with 22 illustrations and 12 tables. Stuttgart: Georg Thieme, 1956. DM 16.50.- $3.95. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Modern Views on the Secretion of Urine: The Cushny Memorial Lectures. Edited by F. R. Winton, M.D., D.Sc., professor of pharmacology, University College, London. 8°, cloth, 292 pp., with illustrations, tables and a frontispiece. Boston: Little, Brown and Company, 1956. $8.50.

Directory for Exceptional Children: Schools—services—other facilities. Edited by E. Nelson Hayes. Second edition. 8°, cloth, 247 pp. Boston: Porter Sargent, 1956. $4.00.

The Labyrinth: Physiology and functional tests. By Joseph J. Fischer, M.D., clinical professor in otolaryngology, Tufts University School of Medicine, and visiting surgeon for otorhinolaryngology, Boston City Hospital. 8°, cloth, 206 pp., with 30 illustrations and 2 tables. New York: Grune and Stratton, 1956. $6.00.

Cancer of the Esophagus and the Stomach. By Owen H. Wangensteen, M.D., professor of surgery and head, Department of Surgery, University of Minnesota Medical School. Second edition. 8°, paper, 144 pp., with 60 illustrations, 9 tables and 2 plates. New York: American Cancer Society, Incorporated, 1956. *(A Monograph for the Physician* — sixth in a series on the early recognition of cancer.)

Proceedings World Congress of Anesthesiologists: Scheveningen, The Netherlands, September 5-10, 1955. Edited and published by the International Anesthesia Research Society. (Official organ of *Current Researches in Anesthesia and Analgesia.*) 4°, paper, 321 pp., with illustrations and tables. Minneapolis: Burgess Publishing Company, 1956.

Tumors of the Cardiovascular System. By Benjamin H. Landing, M.D., pathologist, Children's Hospital and Children's Hospital Research Foundation, Cincinnati, Ohio; and Sidney Farber, M.D., professor of pathology, Harvard Medical School. 4°, paper, 140 pp., with 138 illustrations. Washington, D.C.: Armed Forces Institute of Pathology, 1956. $1.50. (*Atlas of Tumor Pathology,* Section 3-Fascicle 7.)

Tumors of the Thymus Gland. By Benjamin Castleman, M.D., chief, Department of Pathology and Bacteriology, Massachusetts General Hospital, and clinical professor of pathology, Harvard Medical School, Boston. 4°, paper, 84 pp., with 81 illustrations and 4 colored plates. Washington, D.C.: Armed Forces Institute of Pathology, 1956. $1.00. (*Atlas of Tumor Pathology,* Section 5-Fascicle 19.)

Preparing for Motherhood: A manual for expectant parents. By Samuel R. Meaker. M.D., professor emeritus of gynecology, Boston University School of Medicine. 8°, cloth, 196 pp., with illustrations. Chicago: The Year Book Publishers, Incorporated, 1956. $2.00.

Your Blood Pressure and How to Live with It. William A. Brams, M.D. 8°, cloth, 160 pp., with illustrations by Hertha Furth. Philadelphia: J. B. Lippincott, 1956. $2.95.

The Diagnosis and Management of Urological Cases: A handbook for students, residents and general practitioners. By Bruce W. T. Pender, M.B., B.S., F.R.C.S., senior surgical registrar, St. George's Hospital, London; and James O. Robinson, M.A. (Cantab.), M.Chir., F.R.C.S., senior surgical registrar, St. Bartholomew's Hospital, London. With a foreword by Sir W. Heneage Ogilvie, K.B.E., M.A., M.D., M.Chir., F.R.C.S., consulting surgeon, Guy's Hospital, London. 8°, cloth, 170 pp., with 48 illustrations. London: Bailliere, Tindall and Cox, 1955. $5.00. (Distributed in the United States by the William and Wilkins Company, Baltimore.)

Neural Control of the Pituitary Gland. By G. W. Harris, F.R.S., Sc.D., M.D., Fitzmary Professor of Physiology, Institute of Psychiatry, Maudsley Hospital. 8°, cloth, 298 pp., with 54 illustrations. London: Edward Arnold (Publishers) Limited, 1955. $6.75. (Distributed in the United States by the Williams and Wilkins Company, Baltimore.)

Studies in Topectomy. Edited by Nolan D. C. Lewis, M.D.; Carney Landis, Ph.D., D.Sc.; and H. E. King, Ph.D. 8°, cloth, 248 pp., with 26 illustrations and 34 tables. New York: Grune and Stratton, 1956. $6.75. (*Report of the New York State Brain Research Project.*)

Venous Return. By Gerhard A. Brecher, M.D., Ph.D., Julius F. Stone Professor of Physiology, Ohio State University College of Medicine. 4°, cloth, 148 pp., with 55 illustrations and a frontispiece. New York: Grune and Stratton, 1956. $6.75.

Studies from the Rockefeller Institute for Medical Research. Reprints. Vol. 152. 8°, paper, 614 pp., with illustrations, tables, charts and plates. New York: Rockefeller Institute for Medical Research, 1956.

Kohlenhydratstoffwechsel, Insulin und Diabetes. By Prof. Dr. Hans Staub, superintendent, Medizinischen Universitäts-Klinik, Basel. 8°, paper, 48 pp., with 19 illustrations and 6 tables. Stuttgart: Georg Thieme, 1956. DM 9.60.- $2.30. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

The Annual Survey of Psychoanalysis: A comprehensive survey of current psychoanalytic theory and practice. Vol. 3. 1952. Edited by John Frosch, M.D.; Nathaniel Ross, M.D.; Sidney Tarachow, M.D.; and Jacob A. Arlow, M.D. 8°, cloth, 682 pp. New York: International Universities Press, Incorporated, 1956. $10.00.

Leitfaden der Neurologie. By Prof. Dr. med. F. Laubenthal, head, Psychiatrischen und Nervenklinik der Städtischen Krankenanstalten, Essen, and professor, Universität Bonn. Sixth edition, enlarged and improved. 8°, cloth, 315 pp., with 87 illustrations. Stuttgart: Georg Thieme, 1956. DM 29.70.- $7.10. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Klinische Funktionsdiagnostik. By Doz. Dr. Heinrich Küchmeister, Medizinische Universitätsklinik und Poliklinik,

Hamburg-Eppendorf. In collaboration with Prof. Dr. W. Bolt, Köln, Prof. Dr. H. Goldeck, Hamburg, and Dr. H. Hamm, Hamburg. With a foreword by Prof. Dr. A. Jores, Hamburg. 8°, cloth, 410 pp., with 152 illustrations. Stuttgart: Georg Thieme, 1956. DM 49.50.- $11.00. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Säuglings-Enteritis. Edited by o. Prof. Dr. A. Adam, director, Universitäts-Kinderklinik, Erlangen. 8°, cloth, 536 pp., with 43 illustrations and 39 tables. Stuttgart: Georg Thieme, 1956. DM 60.- $14.30. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Die Pflege des gesunden und des kranken Kindes: Zugleich ein Lehrbuch der Ausbildung zur Sauglings- und Kinderkrankenschwester. By Prof. Dr. med. Werner Catel, director, Universitäts-Kinderklinik, Kiel. Fifth edition, improved. 8°, cloth, 655 pp., with 336 illustrations. Stuttgart: Georg Thieme, 1956. DM 42.- $10.00. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Sports Injuries Manual: For trainers and coaches. By Donald F. Featherstone, principal, Athlete's Injury Clinic, Southampton, physiotherapist, Hampshire County Cricket Club, and physiotherapist and trainer to Southampton Speedway Team. With a foreword by R. Salisbury Woods, M.D., F.R.C.S. 8°, cloth, 132 pp., with illustrations. New York: Philosophical Library, 1956. $4.75.

Understanding Human Behavior. By James L. McCartney, M.D. 8°, 258 pp., with 12 illustrations. New York: Vantage Press, 1956. $3.50.

Understanding and Counseling the Alcoholic: Through religion and psychology. By Howard J. Clinebell, Jr. 8°, cloth, 252 pp. New York: Abingdon Press, 1956. $3.75.

Selected Papers of Joseph W. Mountin, M.D. By the Joseph W. Mountin Memorial Committee. 8°, cloth, 356 pp., with a frontispiece. 1956. $5.00. (Available to purchasers through the book service of The American Public Health Association at 1790 Broadway, New York City.)

Cancer: A manual for practitioners. Third edition. 8°, cloth, 321 pp. Boston: American Cancer Society (Massachusetts Division), Incorporated, 1956. $2.00.

The Nurse and the Mental Patient: A study in interpersonal relations. By Morris S. Schwartz, Ph.D.; and Emmy Lanning Shockley, R.N., M.S. in nursing education. With the assistance of Charlotte Green Schwartz, M.A. 8°, cloth, 289 pp. New York: Russell Sage Foundation, 1956. $3.50.

Modern Trends in Orthopedics. (Second Series.) Edited by Sir Harry Platt, LL.D., M.D., M.S., F.R.C.S., F.A.C.S., consultant adviser in orthopedic surgery, Ministry of Health, and president, Royal College of Surgeons of England. 8°, cloth, 331 pp., with 226 illustrations and 12 tables. New York: Paul B. Hoeber, Incorporated, 1956. $12.50.

The Cyclopedia of Medicine, Surgery, Specialties. George Morris Piersol, M.D., editor-in-chief, professor of medicine and director of the Center for Research and Instruction in Physical Medicine, Graduate School of Medicine, and professor of physical medicine, School of Medicine, University of Pennsylvania; and Edward L. Bortz, M.D., assistant editor, associate professor of medicine, Graduate School of Medicine, University of Pennsylvania. 4°, paper, 1150 pp., profusely illustrated with full page color plates and other engravings. Philadelphia: F. A. Davis Company, 1956. (Loose-leaf revision service, 1956.)

Annual Review of Medicine. Vol. 7. Edited by David A. Rytand, M.D., Stanford University School of Medicine; and William Creger, M.D., Stanford University School of Medicine. 8°, cloth, 611 pp. Stanford, California: Annual Reviews, Incorporated, 1956. $7.00.

Leitfaden der praktischen Audiometrie. By Prof. Dr. Bernhard Langenbeck, Bonn. Second edition, improved. 8°, paper, 196 pp., with 52 illustrations. Stuttgart: Georg Thieme, 1956. DM 24.- $5.70.

Symptome und Diagnose der Hals-Nasen-Ohren-Krankheiten. By Prof. Dr. M. Schwarz, director of the Univ.-Hals-Nasen-Ohren-Klinik, Tübingen. 8°, cloth, 351 pp., with 88 illustrations. Stuttgart: Georg Thieme, 1956. DM 48.- $11.40.

Histologie und mikroskopische Anatomie des Menschen. By Prof. Dr. W. Bargmann, professor of anatomy, Universität Kiel. Second edition, improved. 4°, cloth, 796 pp., with 640 illustrations. DM 69.60.-$16.55.

Electrocardiography: Fundamentals and clinical application. By Louis Wolff, M.D., visiting physician, consultant in cardiology and chief of the Electrocardiographic Laboratory, Beth Israel Hospital, Boston, and assistant clinical professor of medicine, Harvard Medical School. Second edition. 4°, cloth, 342 pp., with 199 illustrations and 14 tables. Philadelphia: W. B. Saunders, 1956. $7.00.

1956 Medical Progress: A review of medical advances during 1955. Edited by Morris Fishbein, M.D. 8°, cloth, 389 pp., with 6 tables. New York: The Blakiston Division, McGraw-Hill Book Company, Incorporated, 1956. $5.50.

Gestation: Transactions of the Second Conference, March 8, 9, and 10, 1955, Princeton, New Jersey. Edited by Claude A. Villee, Ph.D., assistant professor of biologic chemistry, Department of Biological Chemistry, Harvard Medical School. 8°, cloth, 262 pp., with 118 illustrations and 8 tables. New York: Josiah Macy, Jr., Foundation, 1956. $5.00.

"Controlled Hypotension" in Anesthesia and Surgery. By David M. Little, Jr., M.D., Department of Anesthesiology, Hartford Hospital, and assistant clinical professor of anesthesiology, Yale University School of Medicine. 8°, cloth, 159 pp., with 14 illustrations and 18 tables. Springfield, Illinois: Charles C Thomas, 1956. $4.50. (Publication No. 283, *American Lecture Series.*)

The Flavonoids in Biology and Medicine: A critical review. By Maurice E. Shils, Sc.D.; and Robert S. Goodhart, M.D. 8°, paper, 101 pp., with 8 illustrations and 8 tables. New York: The National Vitamin Foundation, Incorporated, 1956. $2.00. (*Nutrition Monograph Series,* No. 2.)

The Technique of Operative Surgery: Stomach-duodenum: The operation of the Billroth II type. By Dr. med. Raimund

Wittmoser. English translation by John C. Foster, M.B., Ch.B. (Edinburgh), F.R.C.S. (Edinburgh), senior registrar, Bradford Royal Infirmary. French translation by A. Jost, chief of clinic, Service Universitaire de Chirurgie, Lausanne. 8°, cloth, 350 pp., with 452 illustrations. Vienna: Wilhelm Maudrich, 1955. $12.48. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Die Kausalgie:Ein Beitrag zur Frage der Schmerzen bei peripheren Nervenverletzungen. By Prof. Dr. Med. Erich Trostdorf, physician-in-chief, Univ.-Nervenklinik Göttingen. With a foreword by Prof. Dr. G. Ewald, Göttingen. 8°, paper, 138 pp., with 19 illustrations. Stuttgart: Georg Thieme, 1956. DM 10.50- $2.50. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

Practitioners' Conferences: Held at the New York Hospital–Cornell Medical Center. Vol. 4. Edited by Claude E. Forkner, M.D., professor of clinical medicine, Cornell University Medical College, attending physician, New York Hospital, and consultant in medicine (hematology), Roosevelt Hospital, New York City. 8°, cloth, 410 pp., with 14 illustrations and 14 tables. New York: Appleton–Century–Crofts, Incorporated, 1956. $6.75.

Praktische Gastroenterologie. By Dr. Ernst Hafter, Zürich. With notes by Priv.-Doz. Dr. H. W. Hotz, Luzern, and Priv.-Doz. Dr. F. Deucher, Zürich. 8°, cloth, 380 pp., with 148 illustrations and 1 table. Stuttgart: Georg Thieme, 1956. DM 48.- $11.45. (Distributed in the United States by Intercontinental Medical Book Corporation, New York City.)

NONCLINICAL NOTES

SOUTH'S REGIONAL PROGRAM

Dr. Wilfred Bloomberg, chief of the Psychiatry and Neurology Service of the Boston Veterans Administration Hospital, has accepted an invitation to head the South's Regional Program in Mental Health Training and Research, conducted by the Southern Regional Education Board with headquarters in Atlanta, Georgia. Dr. Bloomberg's appointment as associate director for mental health becomes effective on January 1, 1957.

The Southern Regional Education Board was established in 1949 by legislative action of the 14 southern states. Its Regional Mental Health Program, which Dr. Bloomberg is to direct, was initiated at the Southern Governors' Conference of 1953.

NOTICES

ANNOUNCEMENT

Dr. Francis J. Riley announces the opening of his office at 1268 Wilbraham Road, Springfield, Massachusetts, for the practice of obstetrics and gynecology.

SOLDIERS HOME, CHELSEA

A professional-staff meeting of the Soldiers Home, Chelsea, will be held in the auditorium of the Quigley Memorial Hospital on Wednesday, December 12, at 7:15 p.m. Dr. Louis Weinstein, associate professor of medicine, Boston University School of Medicine, chief, Department of Infectious Diseases, Massachusetts Memorial Hospitals, and lecturer on infectious diseases will speak (subject to be announced).

All physicians are invited to attend.

AMERICAN COLLEGE OF CHEST PHYSICIANS AND OVERHOLT THORACIC CLINIC

There will be a combined meeting of the New England States Chapter of the American College of Chest Physicians and the Overholt Thoracic Clinic in the Joslin Auditorium of the New England Deaconess Hospital, Boston, on Wednesday, December 19, at 4 p.m.

Dr. Bernard L. Brofman will give a talk entitled "The Surgical Management of Coronary-Artery Disease."

All interested physicians are invited to attend.

SCHERING AWARD CONTEST

The Schering Award Committee announces the 1957 Schering Award Contest with an award of $4,500 (first prize $1,000, second prize $500) for papers on three selected topics of current medical significance as follows:

Incidence of Various Types of Cardiovascular Diseases by Age Group in the Male and Female.

Recent Trends in Corticosteroid Therapy for Ocular Disorders.

Recent Advances in the Biochemical Aspects and Treatment of Mental Disease.

In addition to the cash prizes, professionally useful gifts will be offered for other outstanding papers.

Competition is open to all medical students in the United States and Canada. All entries should be submitted by January 1.

Further information and entry blanks may be obtained from medical schools.

INTERNATIONAL FERTILITY ASSOCIATION

The International Fertility Association announces that a special sectional meeting of the North American Fertility Conference, sponsored by the Mexican branch, will be held in Monterrey, Mexico, January 16-19, 1957.

Medical, surgical and psychosomatic aspects will be featured at the bilingual meeting.

Further information may be obtained from Dr. Paul Getzoff, 400 Medical Arts Building, New Orleans 15, Louisiana.

SOCIETY MEETINGS AND CONFERENCES

DECEMBER 7 and 8. Association for Research in Nervous and Mental Disease. Page 923, issue of November 8.

DECEMBER 7–15. Bahamas Medical Conference. Page 923, issue of November 8.

DECEMBER 10. Massachusetts Heart Association. Page 1062, issue of November 29.

DECEMBER 11. 8:00 p.m. Amphitheater D, Harvard Medical School. Dr. Shields Warren, presiding.

DECEMBER 12. Walter E. Fernald State School. Page 728, issue of October 11.

DECEMBER 12. Soldiers Home, Chelsea. Notice above.

DECEMBER 14, 1956, and FEBRUARY and APRIL, 1957. Massachusetts Society for Research in Psychiatry. Page 56, issue of July 5.

DECEMBER 15. International Academy of Proctology. Page 1017, issue of November 22.

DECEMBER 18. Boston City Hospital House Officers' Association. Page 875, issue of November 1.

DECEMBER 19. American College of Chest Physicians and Overholt Thoracic Clinic. Notice above.

JANUARY 16–19, 1957. International Fertility Association. Notice above.

JANUARY 17, 1957. Arthritis Study Unit. Page 831, issue of October 25.

APRIL 27, 1957. Postgraduate Medical Institute. Page 785, issue of October 18.

CALENDAR FOR THE WEEK BEGINNING THURSDAY, DECEMBER 13

THURSDAY, DECEMBER 13

*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.

*8:00–9:00 a.m. Surgical Grand Rounds. Dr. John Spellman and staff. Saint Elizabeth's Hospital.

8:00–9:00 a.m. Medical Journal Club. Joslin Auditorium, New England Deaconess Hospital.

*8:45–9:45 a.m. Cardiac Grand Rounds. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.

*9:00 a.m. Neurological Rounds. Dr. Kane. Evans 2 Conference Room, Massachusetts Memorial Hospitals.

*9:00–10:00 a.m. Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.

*9:00–10:00 a.m. Arthritis Grand Rounds. Robert Breck Brigham Hospital.

*10:00–11:00 a.m. Combined Medical-Surgical Rounds. Sherman Auditorium, Beth Israel Hospital.

*10:15 a.m.–12:00 m. **Medical Grand Rounds. Dr. Keefer. Evans 8 Amphitheater, Massachusetts Memorial Hospitals.**
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Medical Grand Rounds. Dr. Sylvester McGinn and staff. Saint Elizabeth's Hospital.
*11:00 a.m.–12:00 m. Medical Staff Conference. Sherman Auditorium, Beth Israel Hospital.
*11:00 a.m.–12:00 m. Pediatric Conference. Mount Auburn Hospital, Cambridge.
*11:00 a.m.–12:30 p.m. Hand Clinic (Physical Medicine and Rehabilitation Service). Boston City Hospital.
*12:00 m. Clinicopathological Conference. Dr. Benjamin Castleman and associates. Pathology Amphitheater, Massachusetts General Hospital.
*12:15–1:15 p.m. Orthopedic Clinic. Dr. T. W. Botsford. Amphitheater, Peter Bent Brigham Hospital.
*3:00 p.m. Thoracic Conference. Open Heart Surgery. Dr. Dwight E. Harken. Main Amphitheater, Peter Bent Brigham Hospital.
*3:30 p.m. Gastroenterology Conference. Dr. Ingelfinger. Massachusetts Memorial Hospitals.
5:00 p.m. Case Presentation and Pathological Discussion Followed by a Subject of Special Presentation. Joslin Auditorium, New England Deaconess Hospital.

FRIDAY, DECEMBER 14
Massachusetts Society for Research in Psychiatry. Boston Medical Library, 8 Fenway.
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*9:30–11:30 a.m. Medical and Surgical Grand Rounds. Drs. George W. Thorn and Francis D. Moore. Main Amphitheater, Peter Bent Brigham Hospital.
*10:00 a.m. Tuberculosis Surgical Clinic. South End Health Unit, 57 East Concord Street.
*10:00 a.m. Ward Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Medical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*11:30 a.m. Tumor Clinic. Drs. Soutter and Lemon. Robinson 4, Massachusetts Memorial Hospitals.
*12:00 m. Pediatric Grand Rounds. Thorndike Amphitheater, Boston City Hospital.
*12:30–1:30 p.m. Surgical Grand Rounds. Stearns Auditorium, New England Center Hospital.
*1:30 p.m. Fertility and Endocrine Clinic. Free Hospital for Women, Brookline.
*1:30 p.m. Tumor Clinic. Mount Auburn Hospital, Cambridge.
*2:00–3:00 p.m. Pathology Conference. Dr. James Graham. Saint Elizabeth's Hospital.
*4:00–6:00 p.m. X-Ray Conference. Dr. Merrill C. Sosman. Stearns Auditorium, New England Center Hospital.
*4:00–10:00 p.m. Alcoholism Clinic. By appointment. Washingtonian Hospital, 41 Morton Street, Jamaica Plain.
*4:30 p.m. Neuroradiologic Conference. X-Ray Conference Room, New England Deaconess Hospital.

SATURDAY, DECEMBER 15
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:30–10:00 a.m. Orthopedic Staff Conference. Boston City Hospital.
*8:30–10:00 a.m. Surgical Grand Rounds. Drs. Charles G. Child, III, A. J. A. Campbell and staff. First (Tufts) Surgical Service, New Cheever Amphitheater, Dowling Building, Boston City Hospital.
*9:00–10:00 a.m. Anesthesiology Conference. Dr. Benjamin Etsten. Anesthesia Laboratory, New England Center Hospital.
*9:30–11:00 a.m. Surgical House Officers' Conference. Second-Floor Conference Room, Carney Hospital, Dorchester.
*9:30 a.m.–12:00 m. Grand Rounds. Haynes Memorial Hospital, Brookline.
*10:00 a.m. Ward Rounds. Massachusetts Memorial Hospitals.
*10:30 a.m. Teaching Ward Rounds. Ward South 2, Free Hospital for Women.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:00 m. Hematology Conference. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

MONDAY, DECEMBER 17
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*10:00 a.m. Ward Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*11:00 a.m.–12:30 p.m. Staff Conference. Child Psychiatry. By appointment. Conference Room (Burnham 7), Massachusetts General Hospital.
*12:00 m. Staff Meeting. The Elective Surgical Patient — Occupational Hazard for Doctors. Drs. Richard C. Webster and Richard J. Coffey. Lecture Hall, Carney Hospital.
*12:00 m.–1:00 p.m. Tumor Conference. Dr. C. C. Lund and members of the Tumor Board. Dowling Amphitheater, Boston City Hospital.
*12:00 m.–1:00 p.m. Pediatric Clinicopathological Conference. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:00 m.–1:00 p.m. Staff Meeting. Obstetrical and Gynecological. Drs. Abrams and Parker. Evans 8 Amphitheater, Massachusetts Memorial Hospitals.
*12:00 m.–1:00 p.m. Metabolism Conference. Dr. Schwartz. Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. Clinicopathological Conference. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*2:00–3:00 p.m. X-Ray Conference. Dr. William Carey. Saint Elizabeth's Hospital.
*3:00–4:00 p.m. Neuroradiologic Conference. Dr. Bertram Selverstone. Stearns Auditorium, New England Center Hospital.
*4:00–5:30 p.m. Anesthesiology Conference. Chemoreceptors in the Body. Dr. Leroy D. Vandam. Surgical Conference Room, Peter Bent Brigham Hospital.
*4:00–5:30 p.m. Anesthesiology Conference. Dr. Benjamin Etsten. Stearns Auditorium, New England Center Hospital.
*5:00–6:30 p.m. Anesthesiology Group of the Lahey Clinic. Joslin Auditorium, New England Deaconess Hospital.
*7:00–9:00 p.m. Slide Seminar in Pathology. Dr. Edward T. MacMahon. Stearns Auditorium, New England Center Hospital.
*7:00–9:00 p.m. Anesthesia Teaching Conference of Greater Boston. Dr. Buskirk. Auditorium, Jimmy Fund Building, Children's Medical Center, 35 Binney Street.

TUESDAY, DECEMBER 18
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical Grand Rounds. Pathology Conference Room, Carney Hospital, Dorchester.
*10:00 a.m. Ward Rounds. Massachusetts Memorial Hospitals.
*10:30 a.m. Medical Grand Rounds. Main Conference Room (Ground Floor), Lemuel Shattuck Hospital.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*12:00 m.–1:00 p.m. Pediatric Grand Rounds. Burnham Memorial Hospital for Children (Burnham 4), Massachusetts General Hospital.
12:00 m.–1:00 p.m. Mortality Meeting (staff members only). Stearns Auditorium, New England Center Hospital.
*12:15–1:15 p.m. X-Ray Conference. Dr. Merrill Sosman. Main Amphitheater, Peter Bent Brigham Hospital.
*1:00 p.m. Medical Pathological Conference. Massachusetts Memorial Hospitals.
*2:00–3:00 p.m. Hematology Conference. Dr. Mario Stefanini. Saint Elizabeth's Hospital.
*2:00–3:00 p.m. Surgical Pathological Conference. Dr. Sheldon C. Sommers. Evans 8 Amphitheater, Massachusetts Memorial Hospitals.
*5:00 p.m. Surgical Journal Review. Mount Auburn Hospital, Cambridge.
*5:00–6:00 p.m. Service Meeting Followed by Clinical Conference (Medical, Surgical, Obstetric). Faulkner Hospital.
*7:00 p.m. Boston City Hospital House Officers' Association. New Cheever Amphitheater, Dowling Building, Boston City Hospital.

WEDNESDAY, DECEMBER 19
*8:00–8:45 a.m. Case Presentations. Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
*8:00–9:00 a.m. Medical and Surgical Clinic on Diabetic Problems. Deaconess II, New England Deaconess Hospital.
*8:00–9:00 a.m. Surgical Grand Rounds. Auditorium, Carney Hospital, Dorchester.
*9:00–10:00 a.m. Surgical Grand Rounds. Dr. Smithwick. Evans 8 Amphitheater, Massachusetts Memorial Hospitals.
*10:00 a.m. Ward Rounds. Massachusetts Memorial Hospitals.
10:30–11:15 a.m. Lecture on Diabetes for Doctors and Patients by Members and Guests of the Joslin Clinic. Joslin Auditorium, New England Deaconess Hospital.
11:00 a.m. Orthopedic Grand Rounds. Bigelow Amphitheater, White 3A, Massachusetts General Hospital.
*11:00 a.m.–12:00 m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:00 m.–1:00 p.m. Boston State Hospital Psychiatry Seminar. Dreams and Their Relationship to Psychotherapy. Dr. Elizabeth R. Zetzel. Reception Building Auditorium, 591 Morton Street, Dorchester.
*12:00 m.–1:00 p.m. Roentgen Diagnostic Conference. 5th-floor teaching unit, Beth Israel Hospital.
*12:00 m.–1:00 p.m. Neurology, Neurosurgery and Psychiatry Conference. Drs. John F. Sullivan, Justin Hope and Bertram Selverstone. Stearns Auditorium, New England Center Hospital.
*12:00 m.–1:00 p.m. Pediatric Medical-Surgical Rounds. Pratt Lecture Hall, Joseph H. Pratt Diagnostic Hospital.
*12:00 m.–1:00 p.m. Pediatric Clinicopathological Conference. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*12:15 p.m. Vascular Rounds. Drs. Edward A. Edwards and Chilton Crane. D-Main, Peter Bent Brigham Hospital.
*12:30–1:30 p.m. Weekly Staff Review of Autopsies. Dr. William A. Meissner. Joslin Auditorium, New England Deaconess Hospital.
*1:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.
*1:00 p.m. Massachusetts General Hospital Hand Clinic. The Clinics of the Massachusetts General Hospital.
*1:00–2:00 p.m. Surgical Staff Meeting. Dr. Smithwick. Evans Conference Room, Massachusetts Memorial Hospitals.
*2:00 p.m. Rectal Clinic. Peter Bent Brigham Hospital.
*2:00 p.m. Vascular Rounds. Robinson 4, Massachusetts Memorial Hospitals.
*2:00–3:00 p.m. Pediatric Conference for Practitioners. Jimmy Fund Building, Children's Medical Center, 35 Binney Street.
*4:00–5:30 p.m. Fracture Lecture. Boston City Hospital.
*4:00–6:00 p.m. Overholt Thoracic Conference. Joslin Auditorium, New England Deaconess Hospital.
*6:00 p.m. Alcoholism Clinic. Peter Bent Brigham Hospital.

*Open to the medical profession.